Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalDec1937uoft

The University of Toronto Medical Journal

(AN UNDERGRADUATE PUBLICATION)

This journal is published six times a year, November to April, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

$1.50 per volume. 25c. per single copy.

ADVISORY STAFF

Prof. E. A. Linell, M.B., Ch.B., M.D. Manc.
J. Harold Couch, M.A., M.B., F.R.C.S. Edin., F.R.C.S. (C.)
H. H. Hyland, M.D., M.R.C.P. (Lond.), F.R.C.P. (C.)
D. Y. Solandt, M.A., M.D. Prof. G. F. Marrian, D.Sc., Lond.

EDITOR-IN-CHIEF
W. G. Bigelow, B.A., '38.

ASSOCIATE EDITOR
J. H. Belton, '39.

FEATURE EDITOR
R. A. Mustard, B.A., '38.

ASSISTANT EDITORS
J. C. McCulloch, '39. K. C. Greer, B.A., '40.

WOMEN'S EDITOR
Miss L. McClelland, '38.

MANAGING EDITOR
V. R. Perry, '39.

CIRCULATION STAFF
Manager—B. W. Vale, '38.

Assistants— W. J. Reid, '38. W. O. H. Perry, '39. E. M. J. FitzHenry, '40. A. J. Denne, 41. D. W. Parker, '42.

Address all communications to Room 107, Anatomy Building.

Volume XV. TORONTO, DECEMBER, 1937. Number 2

Editorial

A Plea for a Medical Students' Common Room

The idea of a common room for medical students is not a new one. One finds the student acutely aware of the lack of such a convenience and he is often heard deploring the unsatisfactory state of affairs that at present exists in our medical college and hospitals. So long has he existed under his present handicap and so ineffective have been his attempts to rectify the situation that the glamorous idea of actually being able to enjoy the advantage of a common room has become a "Lost Horizon" of mythical student bliss — not for him.

Cannot something be done to improve the existing conditions? It is well known that the faculty are aware of our predicament and on more than one occasion have they made efforts to adjust the situation. We appreciate these efforts and the difficulties that are, no doubt, encountered, yet often wonder that some solution is not possible. Perhaps the matter has not been attacked in the proper manner or possibly the "powers that be" are not fully aware of the significance of our plight. In any event, we take this opportunity to discuss through the medium of this editorial column the problem at hand.

In order to make our discussion clear we must first define what we mean by proper common room facilities. In the first place, it is felt that there should be a common room in both the

medical building and the General Hospital. Perhaps the need is greater in the hospital, for the students in the preclinical years have the advantage of Hart House which, although not as convenient as a common room in the building, particularly on cold winter days, does serve the purpose to some extent. The rooms provided should be of adequate size with proper furnishings and within easy reach of the student who has a few minutes of spare time at his disposal.

The purpose that such a room would serve may be discussed, speaking more particularly of a common room in the T. G. H. At present, the only room the students can call their own is the cloakroom adjoining the lecture theatre. This is a room of moderate size filled, with the exception of a very small space, by racks heavily hung with overcoats. On retiring to this sole retreat, a student either sits down in cramped quarters surrounded by these previously mentioned coats or he stands up by the notice-board, only to be practically swept off his feet by a hoard of students just released from a lecture.

Should a student wish to write up a history which he has taken on the ward, there is no place to do it. If he has just been forced to retire from the ward for half an hour while the patient under investigation eats his meal or is otherwise disposed, he has no place where he can sit down in peace and use his time to advantage. With a few minutes to spare between a long ward clinic and a lecture, he is tempted to go over to "The Club" (Corner Bay and College Streets) and have a cup of coffee instead of being able to sit down in a comfortable chair and read his clinic notes or discuss the cases presented that morning. A common room would be an advantage when one is waiting for a new case or going so far as to speak of luxuries—a place to have a smoke during a heavy day's work.

Like every question, this has its traditional two sides. It may be said that students should make use of all their time in a hospital with so many admirable teaching facilities, or that such a common room would be conducive to loitering. There is truth in both of these statements but it is felt that the advantages to be gained by a common room far out-weigh the disadvantages.

The difficulty in obtaining space is a real one and well appreciated by the students. This brings us to a specific suggestion which we should like to place before the students and the faculty.

It has been suggested that the new faculty room adjoining the lecture theatre may be used as a common room by the students. As far as can be ascertained this room is not used during the day. Would it not be possible to throw that room open for the use of the students during hours which the Hospital Board and faculty felt reasonable? At present the room is unfurnished except for a table and some chairs. In view of this the medical society approved of the idea of furnishing this room in return for the privilege of using it. There may be many factors preventing the operation of such a scheme and we admit no great knowledge of the situation but it is a suggestion which we hope will be considered along with the whole problem.

The Association of Medical Students.

You will see below a message from Doctor "Bill" King who represented our Faculty at the Association of Medical Students Conference last spring. Doctor King's endorsement of this Association, after seeing for himself the nature of the project, should mean much to the student body. He has urged you to read the convention issue of their Journal and I further urge you to read their second issue which has just arrived here and will have been distributed to each student by the time this issue appears.

In these days of change and reform in medical administration, with particular reference to schemes of organ-

ized medicine, it is to our advantage to have a common front and thus to guard the interests of our profession and of society in general.

Dear Friends of the Medical Faculty:

On registration day this fall, each of you received along with numerous and sundry other papers, forms and cards, a small booklet entitled, "The Journal of the Association of Medical Students." Those of you who examined this booklet will know all about the Association; what it is, what its aims are, and how it functions. You may have asked yourselves what it has to do with us here in the University of Toronto far removed from the United States.

My purpose in writing these few words is to answer this question and to stimulate those who have not read the Journal as well as those who have, to take an active interest in the Association, to talk about it among themselves, and finally, through the medium of the Medical Society, to send a large group of delegates to the next Conference to be held in Chicago.

I had the honour last year to be appointed as representative of the University of Toronto Faculty of Medicine at the conference held in Baltimore. Incidentally, I was the only delegate from Canada there and felt somewhat conspicuous. Anything I might give in the way of a detailed report of the proceedings of the Conference would be a drop in the bucket compared to the fine review of the whole thing in the Journal. Once again, let me beg you to take the few minutes necessary to read this Journal so you may be thoroughly acquainted with the Association which is only just now coming to occupy a serious place in the minds of Canadian as well as American Medical students.

I wish to draw attention to the name of the organization: it is such as to include all America, and Canada just as much as the States, Canadian Universities, therefore, which have hitherto had no part in the activities of the Association, can and must participate in them and become themselves active units.

The newly drawn-up constitution states that the purpose of this association is "to join together the Medical students of America on the basis of their common interests and problems, and to assist Medical Education better to prepare students to serve themselves, their profession and society, this education to include social and cultural as well as scientific training." This is a pretty grand purpose, my friends, and in order to achieve it, it is going to take the hardest work and the utmost of co-operation between not only the big Universities of the U.S.A. but also between our University and the other Medical Schools of Canada. Medical Students throughout America have much the same problems and they can never be solved unless an organization of this sort is set up and is recognized officially as the mouthpiece and governing body of the Guild of Medical Students. For we are a guild, just as were the skilled craftsmen of ancient days, and only by concerted action can we make our demands felt and hope to have anything done about them.

The thing that impressed me most about the conference last April was the seriousness of the whole affair, the fine intellectual quality of those who were interested in the project, and the keen interest taken in their doings by eminent men in the Medical Profession and the teaching world. The whole atmosphere was one of earnest thought and purpose and all the delegates seemed to be imbued with an enthusiasm and energy to make their organization one of importance.

I say "their" organization because, being the sole representative from Canada, I felt somewhat of an outsider, a mere visitor looking on. Canada definitely was not a part of the group endeavouring to bring about changes and reforms which concern us as deeply as they do them.

My whole aim, therefore, in writing this letter is to arouse the same interest and enthusiasm among the members of our faculty and among those of the other Canadian Medical Schools. Let's get together, ladies and gentlemen, and form a chapter of our own in this University under the auspices of the Medical Society. To do this we need at least twenty interested students: for every twenty members over this we shall be entitled to another delegate to the convention. In time, if the other schools join with us, it will be possible to form a regional committee for Canada located in any one of the cities where Medical Schools are situated.

Let me urge you all to provide yourselves with the booklets and circulars which are, from time to time, sent out by the Publications Committee of the Association. An attempt will soon be made to form a local chapter in this faculty and when this comes, if it be met by the enthusiastic support of the majority of you, the time and money spent in sending a delegate to Baltimore will not have been in vain.

Thank you,

W. L. M. KING, M.D.

In Memoriam

Dr. E. A. Gray.

Medical Superintendent of Toronto General Hospital for nearly twenty years, Elgin Angus Gray, M.B., died on the 22nd of October, 1937. By his sudden passing, that institution lost a beloved and efficient servant, and every lay or professional member of the staff, a friend.

In particular, his friendship and guidance were bestowed upon the undergraduate in medicine, the interne, and the young practitioner. For them, his unfailing tact and courtesy, his unfeigned interest in their welfare, and his dependable sense of justice and fair play were always available during the difficult days of adjustment to the institutional and public services of the profession. Beneath the ready smile and gentle manner which invited and received the frankest confidences in ethical and administrative problems, there was a quiet insistence upon forthrightness and efficiency as the readiest way to solve those problems With grace and dignity, and without a trace of pettiness or petulance, he shouldered the heavy responsibilities of his office, and earned the respect and affection of all.

Doctor Gray was born near Sarnia, Ontario, in 1878, and graduated from the University of Toronto in 1903. For some years he engaged in general practice in Western Canada. It was in September, 1918, that he received his appointment at Toronto General Hospital. He is survived by his wife and two sons: Elgin Angus, Jr., and Cameron.

MEDICO-LEGAL EVIDENCE

By ROBERT G. ARMOUR, M.B., F.R.C.P. (CAN.)

What I have to say concerning this sphere of the medical man's duties and responsibiliites I say as a doctor, one who happens to have had considerable experience before the Courts, and who is jealous for the reputation of the profession. I am not attempting to expound the law, and though I have tried to be accurate according to what my experience has taught me, I might very well be in some error as to what the law is, and am open to correction.

The view I want to make clear and prominent is that, though we doctors may think that such and such should be the case in the application of medicine to law, such may not be so. The law in such matters has developed through centuries of experience, obviously a far greater experience than any generation of doctors could have had, and one's increasing experience teaches one that the legal profession is probably more competent than we to determine what is right and just, particularly if we will give our testimony simply, as a matter of scientific fact, and without bias.

In the consideration of this subject, the first and most important fact to be kept in mind is that the medical expert enters the witness-box to help the Court, to help the Judge and the Jury, to understand the medical problem involved, in short, to further the ends of Justice. The expert is not an advocate, and should not attempt to argue the case.

Unfortunately, in almost all cases, the expert is engaged by one side or other, and so the latter temptation may be strong. On some occasions counsel for both sides will agree on one expert who is to examine the plaintiff and give evidence as an independent witness. Still more rarely the Judge may himself appoint a witness in whom he has confidence, this procedure possibly indicating that he has been confused, rather than helped, by those who have already testified.

Why should this latter situation develop, and what can be done to prevent it?

In the first place let us consider the meaning of the word Expert. A physician or surgeon, merely because he has graduated from a medical college and has been licensed to practise is not necessarily expert in all branches of his profession.

Now and again one hears in court arguments between counsel as to what constitutes an expert, and the court will make a ruling.

We, as doctors, are not concerned with any such dispute, but as individual practitioners we may be aware that we have not sufficient knowledge, nor had sufficient experience in a certain disease to be able to make any useful contribution, and under these circumstances it is obviously our duty, for the honour of the profession, as well as for the sake of our own conscience, to make our position clear before allowing ourselves to be called, or at the latest as soon as the examination in the witness box takes us beyond our truly expert knowledge. It is really a very distressing sight to see a professional confrere floundering out of his depth under cross-examination by a skilful counsel.

At this point I should like to insist that there is no need for the fear some men have of the witness-box. Cross-examination is no reflection on their veracity. It should only be regarded as a legitimate way of determining whether the witness is sure that what he has said is correct, as to whether he has considered the problem from all angles, and as to whether he is really competent to speak with authority on a given subject.

A reasonable and conscientious man

will be quite willing to change his mind when given additional facts to consider, and will lose none of his reputation by so doing. If fully competent, and if he has told only the truth, he will probably have nothing to retract, but may in cross-examination be enabled to give even more help than he did in examination-in-chief, that is while being examined first by the side which engaged him.

On the contrary, the man who has been too enthusiastic, and has allowed himself to become an advocate rather than a witness, the man who allowed himself to talk about matters in which he is inexperienced, and the man who said what was not true, these men may have to retract and alter what they have said, and may lose much prestige.

Let us consider the relations between the expert and the counsel before entering the court-room.

It is unfortunately obvious that certain medical men allow themselves to be "used" by unethical lawyers. Again other medical men may mislead lawyers by intimating that they are prepared to say certain things that they should know they will not be able to substantiate when confronted with different opinions. I do not mean to suggest that a medical man should be deprived of the right to express his personal opinion based on experience, and to expound his individual conceptions when they differ from the generally accepted views of the majority of the Profession. When he does so, however, he should explain that his personal experience has led him to differ with recognized authorities, and he should admit a knowledge of these other opinions. The Court always prefers to hear his personal opinion, based on his own experience, which is open to cross-examination, rather than to accept portions read out of text books, which are often taken out of their context, and whose authors are not subject to cross-examinations, and so one has little to fear from being frank and reasonable.

A difficulty almost always arises which seems impossible to obviate in view of the established method of conducting cases.

A medical witness often gives an opinion based on certain statements made direct to him by a plaintiff whom he has examined, or through the plaintiff's lawyer.

In the witness box this individual may change his story, or other witnesses may give evidence contradictory to what the medical man has heard up to date. This may necessitate a change of opinion from what this medical man may have previously given to the lawyer who has engaged his services. This change of opinion should be conveyed to the lawyer without delay, and, if possible before the medical witness enters the witness box. By the way, let it be understood that it is no part of the medical man's function to pass on the credibility of any witness. That is entirely the function of the Court, and if the medical witness attempts to usurp it, he may incur a very severe reprimand.

Perhaps, before going any further it should be understood in what capacities a doctor may be called to Court. If he has been in attendance on an individual he may be subpoenaed merely to give evidence as to fact, what disease he treated his patient for, what treatment he administered, what the patient has said to him, and so on. He may, perhaps, not be used as an expert, not asked to give an opinion. He is merely a witness as to fact and is not an expert. Since both sides are restricted in the number of experts they may call without special permission, the medical man should restrict himself carefully to simple answers to questions put to him for fear he make himself an expert and upset the calculations of those calling him.

It must be understood that if subpoenaed, the doctor must answer what relevant questions are asked him, and that professional confidence cannot be pleaded to conceal knowledge that he has obtained from a one-time patient. Of course he may have certain know-

ledge of the patient which he would be unwilling to reveal, and which is not relevant to the case. There is no obligation for him to volunteer this, and it probably will not come out if he confines himself to answering the questions put to him.

Next, a doctor may be asked to give opinion evidence. He may be asked to examine an individual and to render a report to the legal firm requesting this. Bear in mind that this report should be kept confidential. Sometimes the lawyers on the other side may ask for a copy of the report, and, in support of their request, point out that the examination has been carried out on an order of the Court. This may not be strictly true. It may be that the individual, perhaps on legal advice, has refused to submit to an examination, but has been compelled to present himself to such and such a doctor for an examination by an order of the Court. This does not mean that such a doctor must give a report to this individual's solicitor. I believe that the person examined is under the order of the Court, not the doctor. In any case it is always safer to communicate with the legal firm which engages one before giving any information to the other side.

In addition to, or in place of, examining and reporting on an individual the expert, before entering the witness box, may be asked to attend Court, listen to evidence given by other witnesses, medical and lay, and then give the Court his opinion. Let me reiterate that it is not the doctor's function to accept or reject the statements of any of the witnesses, but the question may possibly be put to him, "Assuming that such and such statements are true, what would be your opinion?" Where such evidence has been given by a doctor, other medical witnesses may be asked whether or not they agree with him. One medical witness may say of another medical witness that the latter has not said what is generally accepted by the profession, or what is not true of a certain disease. This constitutes his opinion, and though it may be expressed most emphatically, this should be done with the courtesy that is to be expected between members of a learned profession.

Disputes sometimes arise as to how far a doctor can be compelled to attend Court and give opinion evidence. This dispute frequently hinges on the amount of remuneration a legal firm is willing to offer. Incidentally it is always well to have a clear understanding about remuneration before becoming involved in a case.

It always seems wiser to me to make two financial arrangements, a specified fee for the examination and report, the account for this to be enclosed with the report. If the report does not suit the firm asking for it, they should pay the account and need not call you to Court. But, when first consulted a further agreement should be made as to what fee per day will be paid for your attending Court, listening to evidence, if necessary, and giving an opinion. Under these circumstances you could not be forced into the box to give an opinion for five dollars.

If subpoenaed one should be given five dollars at the time, the legal fee per day for an expert. On this one must attend, but I would not consider he could be compelled to express an opinion. If he has examined the individual he can be compelled for this fee to give his findings at the examination.

I imagine that if the first side does not want to call you and use your opinion, the other side knowing of your examination, might subpoena you and compel you to give the findings of your examination. It is doubtful, however, how far you could be compelled to give an opinion. Your report having gone to the other side and being their property, could not be recovered from you. I do not think the Court would compel you to divulge to the second side what opinion you had given to the first.

As for compelling you to listen to other witnesses and express an opinion on their evidence, I am not aware

by what process you could be compelled to pay attention and listen to anyone, and no one can be compelled to form an opinion on any subject.

It can always be kept in mind that counsels are not anxious to put an unwilling witness into the box, neither are they likely to put in one unless they know what he is going to say.

In connection with this, a doctor is under no obligation to talk until put into the witness box, and ethical questions often arise in the office when lawyers are trying to find out one's opinion before engaging one.

Much of what has just been said has more particular reference to accident cases, and a further word with regard to these cases seems indicated.

The physician or surgeon looking after the average case in his practice is quick and anxious to note any sign of improvement, and to give encouragement by as good a prognosis as he feels is justified. But when his case happens to have been the victim of an accident and a lawsuit is impending, the temptation will be to try and find out all that is wrong, and not to be too optimistic for the future. Naturally one has a responsibility with regard to the future of one's patient, but it is not fair to make only the most gloomy prognostications and not to admit any likelihood of a good recovery ensuing.

In cases of wills being probated circumstances naturally differ. The mentality of an individual now dead is being investigated as at the time at which he made the will in dispute.

In this case the medical witness who had been in attendance at or about the time of the making the will is expected to be able to express an opinion, even though not a psychiatrist, as to his patient's testamentary capacity. There are many legal ramifications that will turn up in such cases, but there are some basic rules that the medical man should know ahead.

In the first place, a doctor having acted as a witness to a will has thereby practically certified to his patient's capacity to make that will.

He may be asked by the testator or his legal adviser, at the time of the making of a will to express a definite opinion on the capacity of the testator, and his opinion should not be formed too lightly.

It should be very carefully determined whether or not there is any degree of aphasia, and if so, whether this is sufficient to deprive the patient of the ability to know exactly what he is doing, speaking, hearing, reading, or writing.

A claim may be advanced that he was unduly influenced. Naturally an old or a sick person will be influenced by those about him, but undue influence has been defined as consisting in fraud or coercion, and the medical man may have to express his opinion as to how easily such a person could have been coerced or defrauded.

Your patient may have been suffering from delusions, but, to upset the will, it must be shown that such delusions influenced the provisions of the will.

There are certain requirements as to testamentary capacity, variously worded in different books, which a medical man should know before expressing an opinion as to capacity. Briefly these are that,

1. He shall know the extent of his possessions.
2. He shall know the natural objects of his benefactions, and their claims upon him.
3. He shall know the nature and effect of his act, that is that he is making his will, and what its provisions are.

These requirements must be met, and it will not be sufficient for the medical man merely to express an opinion based on his own ideas.

Other medical witnesses may be called to support or attack the theory of the testator's competency. They may never have known the individual, but their duty will be to listen to evidence given and express opinions as to whether or not this suggests the exist-

ence of mental disease. It will still be for the Court to determine, however, whether the individual was competent to make a will, depending on whether his mental state conformed to the rules of competency, or as to whether his mental disease affected its provisions.

The matter of "lucid intervals" is usually a contentious one. Many people seem to believe that a person who has suffered from a mental disease cannot make a good will. The law allows of the making of a will by a person previously insane, and even subsequently again insane, if during this lucid interval he is free from such delusions as might have influenced the making of the will, and provided he is otherwise competent.

I am sure we have all seen many mental patients who could transact very good business. It is true that we should always like to have such transactions supervised. In the case of the making of a will this is an even greater possibility, for the making of a will is thought usually to be a simple matter, and its provisions to be based on intentions of longstanding. Furthermore the Courts are influenced by whether or not the document is what they would call "a good will," and so it will appear that the Courts will even accept a will from some people who were actually insane in some degree at the time they made their wills.

A word now on giving evidence in malpractice cases. First and foremost it is to be kept in mind that Medicine is a hazardous occupation. In spite of our best intentions, none of us knows when he may be attacked in this way, and if and when such a day arrives, it would be a comforting thing to feel that one could expect unlimited help, so far as it is deserved, from one's confreres, and to know that one has made no unnecessary enemies.

The law demands, and the public can only expect "reasonable skill and carefulness," and there can be no necessity for any medical expert witness to exercise his ingenuity, or to strain the truth, to convict any conscientious professional brother who has been practising as well as his mental equipment and local circumstances have allowed.

Finally one comes to the consideration of legal responsibility in criminal cases. It is hard to conceive how medical evidence can justifiably be given to lighten or obviate the legal consequences of any antisocial act other than homicide.

If an individual is, through mental deficiency, or disease, a menace to society, the natural steps suggested by the revelation of this deficiency or disease would be life-time restraint; and the offender might get off more easily if he were to omit this medical part of his defence, and to accept the usual sentence for his offence.

Unfortunately this has been one of the means by which medical expert evidence has been brought into ill-repute, doctors allowing themselves to be "used" in endeavours to relieve offenders of paying for their misdemeanours. As a method of treatment, psychotherapy, a proper form of imprisonment for the first offence might do many a psychopath good, and I should like to see members of the medical profession aid the legal authorities in providing mental and physical discipline to psychopaths with criminal tendencies.

The usual type of case, however, in which medical evidence is presented is when the individual is accused of murder, and the defence is insanity.

Provision is here made for a trial within a trial, that is, the issue may be tried as to whether the accused is sane enough to stand his trial before the trial proper for murder is begun.

It should be kept in mind that this preliminary trial has to do only with the accused's mental condition as of the day or days over which the murder trial is likely to extend.

The medical expert would seem to be under no obligation to speak with reference to the condition of the accused as of the time the act was com-

mitted. That will be a part of the defence in the trial proper, and the accused might well expect that this will not be revealed prematurely.

If he is found sane enough to stand his trial, this is immediately proceeded with.

Proof of the existence of a mental disease does not necessarily absolve the accused of the responsibility for his act. His insanity must come under the scope of certain rules, known as the McNaughton Rules. Briefly stated these rules are, (1) Did the accused at the time he committed the act, know the nature and quality of his act? (2) Did he know that it was wrong? (3) Was he labouring under a delusion which, if true, would have justified the act?

Perhaps these rules, if interpreted strictly according to the letter, might seem to offer little protection to many insane homocides. Very few of the most insane patients would not know the effect of plunging a knife into another person, or of the probable consequences of discharging a rifle or other firearm at his head.

A high percentage conform to the ordinary rules of life, whether in hospital or free in the world, and may even give expression to a knowledge of what is commonly regarded as right or wrong in many of the activities of their lives.

Perhaps it might be argued that the only delusion which, if true, would justify killing another would be the fear and conviction held by the insane person that his life had been threatened by the person he killed, but, though I have not space to discuss other possibilities here, I believe this rule can be much more widely interpreted in certain cases.

Many members both of the legal and medical professions have felt that these rules should be brought up to date in the light of more modern knowledge concerning mental diseases.

This is not the place to discuss that matter, nor to indicate how these rules have been interpreted much more widely than was perhaps originally intended. But it is in order, I feel, to say that our judges have, as a rule, been most generous in the application of these rules where the existence of insanity or mental disease has been clearly proved.

A few words of advice as gleaned from remarks of different judges. Naturally, if they think a witness is not truthful, he might better not have appeared at all. They are, however, almost equally distrustful of too enthusiastic a witness. It will soon become obvious if a witness is attempting to argue a case, and this can be made still more obvious if a witness obstinately refuses to admit anything suggested by counsel cross-examining him if the latter carries the process on to a reductio ad absurdum.

The J. F. HARTZ CO., Limited

Carry a complete line of

MEDICAL STUDENTS' SUPPLIES

STETHOSCOPES, OTOLARYNGEAL SETS,
HAEMOCYTOMETERS, HAEMOGLOBINOMETERS.
STUDENTS' DISSECTING SETS

34 GRENVILLE STREET TORONTO, CANADA

THE RELATION OF THE PARATHYROIDS TO BONE DISEASE*

By R. A. GORDON, B.Sc., M.D.

It would obviously be impossible within the limits of this paper to attempt any discussion of all the phases of this interesting subject. I propose, therefore, to confine myself to the development of a conception of the relation of the parathyroids to changes in the osseous system, and to the consideration of the pathogenesis, symptomatology and diagnosis of bone disease resulting from primary hyperparathyroidism. I will also undertake some necessary discussion of the pathology of the osseous changes and a brief consideration of the methods of therapy.

Historical

In 1891 von Recklinghausen studied the bones of two patients with general malacia of the skeleton, and expressed the opinion that the lesions differed from those of osteomalacia. Lesions of a similar kind had been previously described by Engel, Czerny and others, but there had been no differentiation from osteomalacia. In none of these cases was any reference made to the condition of the parathyroid glands. Moreover, the function of these glands was not definitely established until 1896, when Vessale and Generali showed that the removal of the parathyroids without the thyroid resulted in tetany. The first suggestion that there might be an association between the lesions in the bones and the function of the parathyroids came from studies made by Askanazy in 1904, but he failed to associate the parathyroid tumor found in his patient with the lesions seen in the bones.

In 1907 Erdheim reported a case of puerperal osteomalacia in which the parathyroid was enlarged, and showed histological evidence of hyperplasia. Erdheim interpreted the hyperplasia of the glands in these cases as an attempt on the part of the glands to compensate for some defect in ossification, and in defence of this view he pointed to the enlargement of the parathyroids in rickets.

About 1925 Berman, Hanson and Collip, independently, isolated active principles from the parathyroid glands capable of raising the level of blood calcium when injected into normal or parathyroprivic animals, and Greenwald and Aub showed that the hypercalcaemia caused by the extract was followed by an increase in excretion of calcium in the urine.

In the same year Mandl attempted to make clinical application of Erdheims' compensation hypothesis by homotransplantation of a parathyroid in a patient suffering from osteitis fibrosa cystica, but instead of the expected improvement in the bone lesions the clinical symptoms became aggravated. He then explored the region of the thyroid and removed a parathyroid adenoma. The patient began to improve almost immediately, and the urinary excretion of calcium fell abruptly. Mandl's results were confirmed by other observers, and the numerous clinical, metabolic and pathological studies based on reported cases have led to the conception of hyperparathyroidism as a definite entity.

The final link in the chain of evidence linking hyperparathyroidism causally with the osteitis fibrosa cystica of von Recklinghausen came from the experiments of Jaffe, Bodansky and Blair, who showed conclusively that the injection of parathyroid hormone into susceptible animals produced histological lesions in the bones identical in many respects with those seen in von Recklinghausen's disease.

*From a paper presented to A.O.A. Society.

Symptomatology:

Osteitis fibrosa cystica is a rare disease. It is insidious in its development, covering a period of several years, and reaching advanced stages more rapidly in some patients than in others. The symptoms vary, therefore, according to the stage and duration of the disease, and are further modified by complications directly or indirectly attributable to parathyroid hyperfunction. Symptomatology of hyperparathyroidism can, therefore, be discussed only in general terms.

Generally three types of disease may be recognized: (1) The classical form, in which the picture of osteitis fibrosa cystica predominates. (2) The osteoporotic form, with general decalcification of the skeleton and no tendency to the formation of cysts or giant-cell tumors. (3) The metastatic type, in which the chief symptoms are associated with calcium deposition in the soft tissues, notably the kidney. The symptoms of the disease may also be divided, roughly into three groups: (1) Those due to hypercalcaemia per se. (2) Those referable to the skeletal system, and (3) those related to the transport and excretion of calcium.

Symptoms due to Hypercalcaemia: Hyperparathyroidism with its hypercalcaemia is characterized by general weakness, lassitude, and atony, which are the result of decreased response to stimuli. These may be the first signs of the disease and may be mistaken for neurasthenia and hypochondriasis. Hypotonia and difficulty in muscular co-ordination may lead to confusion with lesions of the neuromuscular mechanism. Flat foot and chronic constipation are both of frequent occurrence and are the result of muscular atony.

Symptoms Related to the Skeletal System: These are in the nature of pains in the bones and joints, deformities and fractures. In the early stages of the disease, the pains may be mistaken for manifestations of rheumatoid arthritis, and as the disease progresses, the pain may be so severe that the patient is sensitive even to the pressure of the bed-clothes.

Spontaneous fractures, usually through cystic areas, are not uncommonly the first factor calling attention to the disease. Cysts and tumors in the long bones, giving the appearance of lumps, may also attract attention, and a tumor of the jaw, often treated as an epulis, may be a symptom of hyperactivity of the parathyroids.

Bony deformities occur usually in the later stages of the disease, and vary in nature and extent with the degree of decalcification and cyst formation. The lower extremities are most commonly affected, while the pelvis may be extensively involved and contribute to the distorted position of the lower extremities. The chest may be markedly deformed. Kyphosis and scoliosis are not as common as the deformities of the long bones, but if present, may appear quite early in the disease.

The stature and gait usually reflect the effect of the bony deformities. The gait may vary from a slight limp to absolute inability to walk unsupported, or actual confinement to bed, while the height may diminish as much as ten inches or a foot in the course of a few years.

Symptoms Related to the Transport and Excretion of Calcium: We are concerned with symptoms of this type only in so far as they may point to the possibility of hyperparathyroidism and changes in the bones. Polyuria and polydipsia are present in nearly all cases of hyperparathyroidism. The polyuria is thought to be due to a direct diuretic effect of the parathyroid hormone, and is associated with an increased excretion of electrolytes other than calcium. Enuresis, nocturia and dysuria also occur. Nephrolithiasis and nephrocalcinosis, failure of renal function or renal colic, may be the first indication of the presence of hyperparathyroidism. We will not enter here into any discussion of the mechanism of development of these symptoms.

Diagnosis:

An advanced case of von Recklinghausen's disease presents little difficulty as a problem in diagnosis. Lassitude, muscular hypotonia and other general symptoms related above, with lumps in the bones and spontaneous fractures usually attract attention to hyperparathyroidism. Other cases in which the hypercalcaemia and the gross skeletal changes are not so well marked, may easily be overlooked or confused with a variety of other conditions. The presence or absence of a tumor in the neck is not reliable, since a large parathyroid tumor may exist behind the thyroid or in the mediastinum without being detected, while a palpable or visible tumor is more likely to be an adenoma of the thyroid. Certain laboratory procedures are of assistance in diagnosis of this disease, of which the following are probably the most reliable, but as will be pointed out, by no means infallible:

1. Determination of serum calcium and inorganic phosphorus.
2. Determination of plasma and serum phosphatase.
3. Determination of calcium and phosphorus balance, or urinary calcium excretion.
4. "Hypercalcaemia test in the rabbit."
5. Examination of the bones by X-ray.
6. Examination of biopsy material from the bones.

1. *Serum Calcium and Inorganic Phosphorus:* The concentration of calcium in the serum of normal individuals varies between 9.5 and 11.5 mgm. per cent., and the concentration of inorganic phosphorus varies between 2.5 and 3.5 in adults and between 4.5 and 5.5 mgm. per cent. in children. In typical cases of hyperparathyroidism, the concentration of serum calcium is increased, values between 12.5 and 2915 mgm. per cent. being reported, while the concentration of inorganic phosphorus ranges from 1.5 to 2.5 per cent.

The finding of hypercalcaemia is not infallible, for increased values of serum calcium have been noted in diseases not primarily related to parathyroid hyperfunction, while normal concentrations of serum calcium have been reported in experimental hyperparathyroidism and in cases which are apparently authentic instances of von Recklinghausen's disease. Increased concentration of calcium in the serum is reported in such diseases as multiple myeloma, polycythaemia vera, gout and metastatic carcinomatosis of the skeleton.

The hypophosphataemia of hyperparathyroidism is less constant than the hypercalcaemia. If renal involvement is pronounced, the inorganic phosphorus tends to be increased and the calcium decreased, so that the disease may easily be confused with renal rickets.

2. *Serum or Plasma Phosphatase:* Phosphatase is an enzyme capable of splitting organic phosphorus compounds and liberating inorganic phosphorus. This enzyme is found in all tissues, but in greater quantities in intestinal mucosa, liver, kidneys, leucocytes, in cartilage undergoing ossification and in the connective tissue, in which bone formation is in progress. It is present in only small amounts in the plasma of normal subjects, being somewhat higher in the case of children than in adults. Study of the plasma phosphatase in a variety of diseases has shown it to be abnormally increased in some cases, presenting bone lesions, such as active rickets, osteitis deformans, and osteitis fibrosa cystica, as well as in liver disease. Bodansky gives normal values expressed as units per 100 c.c. of serum as follows: Children 5-12 units; adults 1.5 to 4 units. One unit is the phosphatase activity required to liberate 1 mgm. of phosphorus in one hour under stated conditions.

3. *Calcium and Phosphorus Metabolism in Hyperparathyroidism:* It is not my intention to discuss this at great length here. Briefly, in normal

persons, 70-90 per cent. of the calcium excreted by the body is found in the feces, and very small amounts in the urine, whereas in those suffering with hyperparathyroidism, not only is the total excretion increased, but the paths of excretion are so changed that from 70-90 per cent. is being eliminated in the urine.

The excretion of phosphorus is not as characteristic as that of calcium, but in the main usually parallels the loss of calcium. The balance of calcium and phosphorus is also negative or abnormal in active rickets and osteomalacia; but in these the loss is chiefly by the bowel.

Balance experiments are impractical clinically, but the study of calcium metabolism may be simplified by the study of the urinary calcium excretion alone. Normal individuals receiving about 0.1 gm. of calcium daily excrete about two-thirds of their intake, whereas patients with hyperparathyroidism excrete a great excess over their intake in the urine alone. Such typical urinary findings occur only in those cases which are without complications in the urinary system. In those with renal impairment, the urinary findings may be within normal limits.

4. *"Hypercalcaemia Test" in the Rabbit:* This is a test recently proposed for the measurement of parathyroid hormone present in biological fluids. The fluid to be tested is injected intramuscularly in a rabbit and the blood calcium curve of this animal is compared with that obtained in an animal who receives an injection of a known amount of parathyroid hormone, under stated conditions. It has been found negative in cases of Paget's disease, myositis ossificans, and in solitary bone cysts, and positive in cases of primary hyperparathyroidism and renal rickets.

5. *Examination of the Bones by X-ray:* The appearance of the bones in hyperparathyroidism vary with the degree of parathyroid hyperfunction, the duration of the disease, and the situation of the areas of decalcification with relation to posture and weight bearing. The radiological recognition of advanced cases of osteitis fibrosa cystica should be comparatively simple. The greatest difficulty is in the differentiating the early case, or the osteoporotic form of the disease from osteoporosis unrelated to hyperparathyroidism.

As the name generalized osteitis fibrosa cystica implies, any bone in the body may be involved in the process of demineralization. Cysts, giant cell tumors, and fractures are only secondary changes. With reference to the changes found, I quote Shelling:

"The long tubular bones usually show progressive cortical thinning, with or without expansion of the medullary cavity. Giant cell tumors and well-defined cysts, which are frequently trabeculated and surrounded by shells of bone, may be noted in any part of the diaphysis. Fractures may be seen in the rarefied shaft or in the site of a cystic area. Such fractures tend to unite very readily, but show no excess callus formation. In children and in young adults, the destructive areas tend to localize near the growing ends of the bones, so that the metaphyses may be widened and be suggestive of late rickets—or the epiphyses may slip——."

The skull may be thinned, or it may be thickened generally or irregularly. The teeth may be loosened, but the tooth structure appears not to be affected.

The vertebrae may be normal, or the bodies may be generally osteoporotic or mottled, or softened and collapsed, so that they appear as flattened concave discs.

6. *Pathological Anatomy and Histology of von Recklinghausen's Disease:* Recent studies of experimental hyperparathyroidism in animals and biopsy material from cases of osteitis fibrosa have shown that hyperfunction of the parathyroids may produce a variety of lesions, ranging from extreme decalcification of the skeleton with the formation of cysts, giant cell tumors, and multiple fractures, to changes so slight that only histological examination

demonstrates osteoporosis. Even in severe cases with bone cysts and giant cell tumors, other bones may show no gross evidence of involvement.

The long bones usually show the greatest degree of involvement, and next in order, the spine, pelvis, jaw, and thoracic flat bones. The greatest amount of destruction and repair usually occurs in the diaphysis of the long bones, the epiphysis showing only osteoporosis. The shafts are irregularly expanded and may be deformed in all directions. The bones usually bend very easily and may be cut with a knife. On section, the shaft may show areas of more or less normal marrow, and other areas traversed by fibrosis and cysts of varying size, with complete obliteration of the marrow cavity. In and between the cystic spaces, areas of haemorrhage may be seen, and brownish discoloured areas which are giant cell tumors. The periosteum surrounding the bone in advanced lesions is thin, and there is no periosteal reaction, such as is seen in osteomalacia and rickets. The areas of fibrosis may contain finely reticulated bone. It is evident that the tendency to absorption and decalcification exceeds the tendency to new bone formation, thus distinguishing osteitis fibrosa from Paget's disease.

Histologically, there is replacement of the original bone and the marrow spaces by fibrous tissue, and an abundance of osteoclasts. Some of the areas of fibrous tissue contain immature bone. In the fibrous areas free of bone tissue, multinucleated giant cells and extravasated blood are seen. The abundance of osteoclasts is a prominent feature of the disease. In places where new bone is formed, they usually outnumber the osteoblasts. Newly formed bone undergoes rapid absorption, and numerous osteoclasts are seen clustered about small fragments of the trabeculae. In areas where resorption is not active, the newly formed bone is surrounded by a narrow rim of osteoid tissue, but these osteoid borders are in no way comparable with the wide osteoid borders characterizing rickets and osteomalacia.

In advanced cases of osteitis fibrosa, some of the areas of fibrosis may show brown areas which, on examination, are found to be composed of nests of giant cells, and are known as "giant cell tumours." These may vary in size from minute microscopic lesions to tumors the size of a child's head, which expand part or the whole of the circumference of a long bone. These tumors are usually located in the metaphysis. Histologically, they are composed of a spindle-cell connective tissue stroma with giant cells, which appear to be identical with the osteoclasts, except that they show phagocytosis of red blood cells and hemosiderin. The prevailing opinion is that these are not true tumors, but that the giant cells are probably specialized cells reacting by phagocytosis to haemorrhages, which occur in fibrosed marrow. These tumors may degenerate and become cystic.

Pathogenesis of Osteitis Fibrosa Cystica

Numerous theories and hypotheses are current relative to the pathogenesis of bone resorption in hyperparathyroidism. Some of these theories explain the process purely from the standpoint of the solubility of calcium phosphate in the blood, others explain it as a local reaction in the osseous tissue, while others consider the role of both the local and chemical factors.

Greenwald and Gross have suggested that the parathyroids elaborate an organic substance, which may be parathyroid hormone, capable of forming a soluble, but unionized, compound with calcium; and that such a compound by allowing for a greater solubility of calcium in the blood, shifts the equilibrium of calcium from the bones to the blood, causing decalcification. The simultaneous injection of calcium and parathyroid hormone does not produce a parallel increase in calcaemia, as would be expected from a consideration of this theory. Moreover, such an

organic compound has never been proved to exist in the blood, either of normal individuals or those suffering from hyperparathyroidism.

Allbright suggests that the primary effect of the parathyroid hormone is the lowering of the renal threshold for the excretion of phosphate, leading to a subsaturation of calcium in the serum, and a resultant mobilization of calcium from the bones. Such an explanation merely recounts the changes in concentration of the calcium and inorganic phosphorus in the serum, which may be entirely secondary to the changes in the bones, and fails entirely to account for the cases of osteitis fibrosa with renal impairment as a complication, where a hyperphosphataemia exists. From the occurrence of metastatic calcification in hyperparathyroidism, there is sufficient reason to believe that the blood might rather be supersaturated with respect to calcium phosphate. Like the first theory, this hypothesis also fails to take into consideration the numerous histological phenomena seen in the bones.

Thompson and Collip hold that the most acceptable theory of the action of the parathyroid hormone is that it stimulates the osteoclast to erode the bone. A study of bones in various stages of experimental hyperparathyroidism has frequently revealed that decalcification occurs before the appearance of the osteoclasts, and that only after the lime salts have been sufficiently absorbed do these cells become numerous, in which case they function as phagocytes.

Jaffe attempts to explain the decalcification in hyperparathyroidism by a correlation of the chemical findings in the blood and urine with the histological picture in the resorbed bones. He believes that when the state of hyperparathyroidism is initiated, the minerals are first withdrawn from the soft tissues and excreted, and that the loss of minerals, and also the acidosis which hyperparathyroidism produces, "require compensation through the withdrawal of large stores of earthly alkaline substances from the bones. . . . . Following this decalcification, osteoclasts proliferate to phagocytose the decalcified bone matrix, and marrow fibrosis ensues as part of the reaction to the changed status of the bone structure. It is evident that the continuation of such a state (chronic hyperparathyroidism, whether clinical or experimental) leads to further decalcification, more pronounced resorption through osteoclastic proliferation and additional marrow fibrosis,—all of which produce the advanced pathological picture seen in von Recklinghausen's disease." Jaffe also says, "there is reason to believe that in hyperparathyroidism the tissue fluids circulating about the bone are so changed and modified as to favour removal of minerals from the bone rather than their deposition." We cannot enter here into a lengthy discussion of what these changes may be. There is no doubt, however, that parathyroid hormone increases the solubility of calcium salts in the blood, and that such a change presupposes a change in equilibrium between the bones and the blood in the direction of the latter.

SUBSCRIBERS ARE RESPECTFULLY REQUESTED TO PATRONIZE FIRMS ADVERTISING IN THE JOURNAL.

MEDICO-LEGAL VALUE OF BLOOD GROUPING TESTS IN CASES OF DISPUTED PATERNITY

By ARTHUR J. VON WERSSOWETZ DE BYSTRICE, B.A., '38

Recent years have brought about a more close relationship between the medical and legal professions. This association is a very happy one, indeed, and most fortunate, for it facilitates the work of our legal friends and offers means of their taking advantage of the recent and important achievements in medicine. But alas, the tremendous advance of medical research has made it almost impossible for individuals outside of the profession to keep abreast of these advances. Because of this, some very valuable contributions to medical science of forensic nature have not yet found their recognition in the legislations of many countries.

It is the author's purpose, by means of this article, to bring before the medical profession the legal values of one of these deplorably neglected and perhaps, misunderstood at times, achievements of medical research, namely: the value of blood grouping tests in legal medicine.

By first presenting the facts to the medical profession it is hoped that the value of these tests will become known to the public at large who, after all, learn much from their physician. Once the public is well and intelligently informed, necessary changes will have to take place in the legislation and new bills will have to be enacted, which is exactly the necessity of the moment in the Province of Ontario. According to the existing legislation in Ontario in cases in which blood grouping tests might supply valuable evidence, the Court cannot compel the parties concerned to have their blood groups determined. Introduction of such a ruling into the Ontario legislation would be a notable advancement in its "modernization." This is the more obvious, since blood grouping tests are no longer the exquisite field of the immunologist or the transfusion specialist. They are now recognized and used in the Courts of very many countries in cases of disputed paternity, questioned identity of infants in ward nurseries, feigned maternity, non-parentage, etc.

In 1900 and 1901, Karl Landsteiner and his co-workers showed that there are present in the human blood and serum certain agglutinogens and agglutinins which they called: agglutinogens A and B, and agglutinins α and β, respectively. Subsequent work of Jansky led to his forming a table of four blood groups which he called I, II, III and IV. At about the same time Moss made his classification with the difference that his Group 1 corresponded to Jansky's Group IV. To avoid misunderstanding a new nomenclature was adopted which is now the international one and is: O, A, B and AB, and it corresponds to Jansky's Groups I, II, III and IV, respectively.

Agglutinogens A and B are found in the human red blood cells and agglutinins α and β in the human serum. It was determined that different combinations of these factors may exist. The agglutinogens are agglutinin-stimulating substances and cannot exist simultaneously with the corresponding agglutinins in the blood and serum of the same individual, e.g., if an individual has the agglutinogen A present in his red blood cells, agglutinin α cannot be present in his serum. On basis of this the following table 1 can be made, which will clearly show the different and possible combinations:

It will be noted that Group O has no agglutinogen present, while Group AB has both of them.

Haemoagglutination is among the few serological reactions which are inherited according to the Mendelian law.

Table 1.

Jansky group	Intern'l group	Agglutinog's in RB Cells		Agglutinins in Serum	
I.	O.	—	—	α	β
II.	A.	A.	—	—	β
III.	B.	—	B.	α	—
IV.	AB.	A.	B.	—	—

NB. The "—" sign denotes the absence of the given factor.

Agglutinogens A and B behave, therefore, as Mendelian dominates and are controlled by some factors which are called genes. These genes occur always in pairs and are localized in the chromosomes in the nuclei of the body cells. Each body cell, according to recent investigators, contains 24 pairs of chromosomes, but the male and female germ cells, when mature, have only half the number of chromosomes present, and consequently a half set of genes. The union of the male and female germ cells forms a new cell in which there is a full number of chromosomes and of genes, but a half set from each parent. Now, depending on whether on each pair of chromosomes there is a gene for A or for B present (or absent as in O group), the blood group of the new individual is determined. This permits of the recognition of 6 different genetic formulae, i.e. types. An example will explain: An individual may have the gene for A and the gene for B present, his type then would be AB. On the other hand, he may carry the genes for A by one chromosome and none by the others O; this puts him in the genetype AO. Thus we can distinguish the forementioned 6 genetypes: AB, BB, BO, AA, AO and OO. From this it would follow that there are 2 types of individuals in group A, i.e.: AA, or AO, who show the presence of agglutinogen A in their blood. This depends on whether both chromosomes carry a gene for A (genetype AA), or only one (genetype AO). The same is true of BB and BO. The AA (or BB) is a "pure" type and is called the homozygous, while the other AO (or BO) is the heterozygous. Although theoretically the difference between homozygous and heterozygous types exists, serologically these two cannot be distinguished by laboratory tests. Hence we recognize only four blood groups or phenotypes; O, A, B, AB.

From the fact that each mature germ cell carries only a half set of genes, it is possible to tell the possible genetype of the new individual formed by the union of the male and female germ cells. A male of Group AB has two types of germ cells, one which will carry genes for A and the other genes for B. If the female is of the same Group AB, her germ cells will also carry the same two genes. By the union of these germ cells we can have the following combinations:

Table 2.

Male	Female	Offspring	
gene A	gene A	genetype AA	....25%
gene A	gene B	genetype AB	....50%
gene B	gene A	genetype AB	
gene B	gene B	genetype BB	....25%

Thus in a number of matings of two such parents we would expect to have 25% of the offsprings of genetype AA, 50% of genetype AB and 25% of genetype BB. If we express that in blood groups it would be phenotypes:

A..... 25%
AB..... 50%
B..... 25%

Let us, however, take an example of an AB father and an O mother. By the same number of combinations we get offspring as in Table 3.

Thus it is obvious that 50% of the offspring will be Group A and 50% Group B, but no offspring could be of

Table 3.

Male	Female	Offspring	
gene A	no gene	genetype AO	....50%
gene B	no gene	genetype BO	....50%

the blood group AB, since such a combination is impossible.

But in cases of the father being of the genetype AO and the mother BO, we can get the following combinations:

Table 4.

Male	Female	Offspring	
gene A	gene B	genetype AB	
gene A	no gene	genetype AO	
no gene	gene B	genetype BO	
no gene	no gene	genetype OO	ana 25%

Such a combination of parents can give all four blood groups in the offsprings. But since we cannot serologically recognize between a "pure" homozygous AA group and a heterozygous group AO, we have to accept that the above mentioned combination has to be accepted also when the parents' blood groups are classified only as phenotypes A and B.

Based on these combinations are two laws:

1. Agglutinogens A or B cannot appear in the blood of a child unless present in the blood of one parent.
2. If one parent is of group O, he cannot have a Group AB child, and similarly an AB parent cannot have a Group O child.

This brings us to the question of possible and impossible children from a given set of parents. Reasoning along the same lines as given in Tables 2, 3 and 4, we can set a final table:

Table 5.

No. Parent's group	Possible children	Impossible children
1. O x O	O	AB, A, B.
2. O x A	A, O	AB, B.
3. O x B	B, O	AB, A.
4. O x AB	A, B	AB, O.
5. A x A	A, O	AB, B.
6. A x B	AB, B, A, O	—
7. A x AB	AB, B, A	O.
8. B x B	B, O	AB, A.
9. B x AB	AB, A, B	O.
10. AB x AB	AB, A, B	O.

Studying the above table, it can be seen that in a few cases several sets of parents can have the same sets of possible children. (viz.: Table 5, No. 7, 9, 10; or 2 and 5, etc.)

However, in spite of these limitations the above tests were adopted in 1924 in the German Courts as the basis of evidence in cases of disputed paternity.

In 1928, however, Landsteiner and Levine published the results of their new tests and revealed that there are present in the human red blood cells two more agglutinable substances which are not related to any agglutinins present in the human serum. These 2 new agglutinogens, also inherited as Mendelian dominant characters and demonstrated by the use of immune rabbit serum, were called agglutinogens M and N. Unlike the agglutinogens A and B, the M and N agglutinogens cannot be absent from any type of human blood, at least one being present. Hence we have 3 new phenotypes MM, MN and NN.

It was later found that the M and N factors occur in human blood inde-

pendently of the agglutinogens A and B. This offered a new set of combinations to eliminate the confluent sets referred to in Table 5, consequently doubling the possibilities of determining paternity.

A similar table can be made of possible and impossible children for a given set of parents, using the M and N factors:

Table 6.

Parents	Possible children	Impossible children
M x M	M	MN, N.
M x MN	M, MN	N.
M x N	MN	M, N.
N x N	N	M, MN.
N x MN	N, MN	M.
MN x MN	M, MN, N	—

Two laws necessarily follow from the above table (Wiener and Vaisberg):

1. Agglutinogens M and N cannot appear in the blood of a child unless present in the blood of one or both parents.
2. A type M parent cannot have a type N child, and an N parent cannot have an M child.

The legal value of the A, B, M and N factors in determining non-paternity, false maternity, interchange of infants, etc., can be well illustrated by citing a few Court cases:

Before the Court of Common Pleas of New Haven County on Jan. 17, 1933, the following case was tried: (Wiener).

A woman was accusing a certain man of the paternity of her child. Blood tests were ordered and from these it was found that the blood groups of the woman, alleged father and child were as follows:

Mother: Group O.
? Father: Group A.
Child: Group B.

By consulting Table 5 (No. 2) we see that for a set of parents of Group O and A respectively, the possible children are of groups A or O, the impossible children are of groups AB and B. In the above cited case these conclusions were reached and the man was exonerated, the Court arguing that the real father of the child had to be of the Group B or AB. (Table 5, No. 3 and 4).

Let us, however, for a moment suppose that by the use of the A and B tests it was shown that the man was of the Group AB or B and a possible father of the child. This fact would change the decision of the Court, because in the real case it could definitely be proved that the man cannot possibly be the father of the child, whereas in the last instance all that can be said is that he might be the father.

It is here where the M and N factors become of value. If the A and B tests make the case undecided, there still is the possibility that the M and N factors may eliminate the confusion. Here is an imaginary example:

Mother: Group O; and Group M.
? Father: Group AB, and Group N.
Child: Group B, and Group M.

It can be seen that the M and N combination of parents (Table 6) can only give progeny of MN groups. Therefore, the man in this case could not be the father of the child.

Space does not allow to cite any more examples. However, let us now consider the possibilities and chances of an accused man in proving his non-paternity. These chances, of necessity, depend on the blood group of the man and the corresponding percentage-distribution of this group among the population. Omitting, however, this and taking an average of them all, we can say that with the use of the A and B tests the chances are 1 in 7. But by adding the facilities of the M and N tests, we get the chances increased to 35% or 1 in 3. This is quite remarkable, if we consider that one man out of three, if innocent, can be acquitted in Court and not be forced to pay for the up-keep of an illegitimate child.

The value of these tests is much greater in cases of interchange of infants in the wards. This is due to the fact that the tests are available on the 4 parents and the 2 infants and hence the easy elimination. The chances of settling such a dispute are 3 in 4. All of us will most likely remember the Watkins case of several years ago, when two infants were interchanged in the wards. Their parents were determined by the use of these tests.

In cases of false-maternity, where a woman has feigned pregnancy and labour, using the substitute child for purposes of blackmailing or obtaining inheritance, the possibilities for the alleged father are about 87%.

Summary.

Due to the limitation of space, only a brief review of the blood grouping tests and their forensic applications has been presented. An attempt has been made to emphasize the value of the A, B, M and N factors in these tests in cases of family descent and blood relation.

It has been shown that:

1. In certain cases of alleged paternity it can be determined by means of these tests beyond any doubt that a certain man cannot be the father of a given child;
2. On the other hand, it must be remembered that in no case is it possible to prove a certain man to be the father of a given child;
3. In many countries the Courts now accept evidence based on these tests;
4. There remain, however, many countries in which even the four classical blood groups are not accepted as convincing evidence in Court. Several reasons may account for this fact:
   (a) many of the laity and members of the legal profession are not acquainted with the existence of these tests, or of their practical applications;
   (b) because of the extravagant statements which have been made in the past, in some Courts these tests are still regarded with suspicion;
   (c) for this reason also many individuals may fear to submit to these tests.
5. A real effort should be made to introduce into the Ontario legislature some measure which would authorize the Courts to compel the litigants to submit to these tests.

REFERENCES

Landsteiner, K.: Zentralbl. f. Bakteriol., 1900, 27, p.361.

von Dungern, E., and Hirschfeld, L., Ztschr. f, Immunitats u. exp. Therap., 1910, 6, p.284.

Landsteiner, K., and Levine, P.: Jour. Exper. Med., 1928, 47, p.757.
Ibid., 1928, 48, p.731.
Jour. Immunol., 1929, 16, p.123.

Schiff, F.: Zentralbl. f. Bakteriol., 1929, 30, 96, p.336.

Waugh, Theo. R.: Canad. M. A. J., 1928, 18, p.64.

Hooker, S. B. and Boyd, Wm. C.: Jour. Immunol., 1929, 16, p.451.

Wiener, A. S. and Vaisberg, M.: Jour. Immunol., 1931, 20, p. 371.

Weiner, A. S.: Ibid., 1931, 21, p.157.

Wiener, A. S., and Rothberg, S., Fox, S. A.: Ibid., 1932, 23, p.63.
Ibid., 1933, 24, p.443.
Amer. J. Med. Sci.: 1931, 181, p.605.
Ibid., 1933, 186, p.257.
Canad. M. A. J., 1935, 32, p.393.

Hyman, Harriet S.: Jour. Immunol., 1935, 29, p. 223.

Dujarric de la Riviere, R. and Kossovitch, N.: Ann. Inst. Pasteur, 1935, 55, p.331.

Getter, A. O. and Kramer, H. E.: Jour. Immunol., 1936, 31, p.321.

Harley, D. and Lynch, G. Roche, Brit. Med. Jour., Jan. 23, 1937, p.163.

Ruzicka, V. E.: Uplne biol. predn., Prague, 1930.

The author wishes to express his appreciation to Dr. I. H. Erb for his helpful criticism and the re-reading of this article.

CYANOSIS

By J. W. P. GARRETT, '38.

It is the purpose of this paper to discuss briefly the clinical occurrence and significance of cyanosis, in such a way that it may be useful to the student in his clinical work. An effort will be made to present the factors behind the occurrence of cyanosis, by a short summary of the underlying physiology, keeping figures to a minimum. This will be followed by a clinical classification, with a reference to the important causative factors in each case.

Definition: By the term cyanosis is meant a bluish tinge or colour of the skin and mucous membranes. This change in colour is due to an abnormal change in the circulating blood as it passes through the capillary vessels. This colour change can be obliterated by pressure which forces the blood out of the region where the pressure is applied.

Physiology

The change which usually is responsible for the development of cyanosis is the presence in the peripheral capillary vessels of an abnormally great amount of reduced haemoglobin. For cyanosis to be seen there must be at least 5 grams of reduced haemoglobin per 100 cc. of blood in the capillary blood stream. Since normal blood contains approximately 15 grams of haemoglobin, it follows that an individual who has an anemia, in which the Hb% is less than 33%, cannot develop cyanosis because his blood contains less than 5 grams of Hb per 100 cc. of blood.

Certain other normal blood values which aid in the study of cyanosis are given in the following table, the values given are average figures.

Arterial Blood

Oxygen content 19 cc. per 100 cc. blood	
Per cent saturation	95%
Per cent unsaturation	5% or 1 volume of unsaturation per 100 cc.

Venous Blood

Oxygen content 12 cc. per 100 cc. blood	
Per cent saturation	60%
Per cent unsaturation	40% or 7 volumes of unsaturation per 100 cc.

Capillary blood unsaturation is represented as the average between arterial unsaturation and venous unsaturation. In the average normal figures given above the capillary unsaturation is $\frac{1+7}{2}=4$

If this value is higher than 6, cyanosis appears.

While the amount of reduced haemoglobin is the primary factor in causing the appearance of cyanosis, the depth of colour which is seen may be influenced by other factors. These are pigmentation of the skin, thickness of the skin, the degree of capillary dilation which is present, or the presence of unusual amounts of fatty or pigmentary material in blood plasma.

Factors Producing Cyanosis: There are two main factors which are responsible for the amount of reduced haemoglobin which is present in the peripheral circulation. These are:

i. The degree of oxygenation which the blood undergoes in the lungs.
ii. The state of the peripheral circulation, or in other words, the amount of oxygen desaturation which occurs in the capillary circulation.
iii. In addition to these two factors, there may be some condition of the blood itself which tends to produce the cyanotic hue.

1. If for any reason there is inadequate oxygenation of haemoglobin, while in the lungs, then the arterial blood which returns to the left side of the heart and is sent out into the systemic circulation is

more unsaturated than normally. In the tissues, the normal loss of oxygen from the blood occurs with tissue respiration and this further unsaturation added to that already present may bring the capillary unsaturation value to the threshold level at which cyanosis appears.

2. Any condition which tends to cause obstruction of venous blood flow, or a decreased capillary rate of flow, with a tendency to peripheral stasis may cause cyanosis. The decreased rate of flow allows the blood to remain longer than normally in contact with the tissues. As a result of prolonged gaseous exchange, much more oxygen is given up by the blood and as a result, capillary blood unsaturation reaches the threshhold level and cyanosis develops.
3. There may be cyanosis due to the presence in the blood of abnormal pigments. The most common of these are methaemoglobin and sulphaemoglobin.

Clinical Considerations

Cyanosis while an important sign to be observed, is rarely the only sign of disease present. Usually, in any serious disease, by the time that cyanosis is present, there are other significant signs or symptoms which aid in making a diagnosis. Cyanosis is a sign which may be due to many causes; accurate diagnosis of that cause is important in order that treatment may be applied.

The bluish colour of cyanosis becomes apparent first where the circulation is poorest in the affected part. Such regions as the ears, lips, fingers and toes are first affected.

Cyanosis as a clinical condition may be

1. local
2. regional
3. general

These conditions will now be considered separately in more detail.

Local Cyanosis

Local cyanosis of a mild type is relatively common. It is seen in the hands and feet when those parts have been exposed to cold which has caused slowing of the blood flow but not complete arteriolar spasm.

Raynaud's Disease: A vaso spastic disturbance of the digital arteries. occurring intermittently and brought on by exposure to cold, often with associated emotional stimuli. There is bilateral symmetrical distribution with pallor or cyanosis. Advanced cases have some residual cyanosis between attacks. The cyanosis is due to capillary stasis, since there is arteriolar spasm decreased pressure to force the blood through the capillaries.

Buerger's Disease: This is a chronic disease of the extremities, usually the legs characterized by a combined arteritis and phlebitis with patches of thrombosis. Cramp-like pains develop in the calf on exercise and this intermittent claudication is usually followed by the development of redness or cyanosis when the legs are dependent. This is due to capillary and venule engorgement due to loss of tone in these vessels and also decreased force getting through from the arteries with resulting less efficient drainage.

Regional Cyanosis

Cyanosis which invokes a large part of the body but which is limited to that part of the body is not common. Two examples may be given—

1. *Superior vena caval obstruction*: A mediastinal tumour or thoracic aneurysm may compress the superior vena cava and produce a cyanosis which involves the head, neck, arms and shoulders. There may or may not be other signs of mediastinal pressure. The cyanosis is due to obstruction of venous drainage with peripheral congestion and increased reduction of haemoglobin in the capillary blood.

2. *Obstruction of a large artery*: Acute occlusion of a large artery produces a typical picture. There is usually

sudden pain at or distal to the site of lodgement of the embolus. On examination there is numbness, coldness and either a waxy pallor or a blotchy cyanosis extending up to within a hand's breadth of the site of the occlusion. If cyanosis is present it is due to stasis of blood in the tissues due to loss of the pressure to force it onward.

General Cyanosis

In many ways general cyanosis is of considerable importance as it is commonly indicative of serious disease. It tends to appear first in the lips, ears, fingers and toes and spreads from those parts as it becomes more marked.

For purposes of study and classification, the causes of cyanosis can be divided into three groups. These groups are:

A. Haematogenous causes
B. Cardiac causes
C. Respiratory causes

A. Haematogenous Causes:

i. Substances other than reduced haemoglobin may cause cyanosis. Of these the most important are methaemoglobin and sulphaemoglobin. They occur in cases of chronic poisoning by potassium chlorate, or by coal tar products and of the latter especially acetanilide. The presence of the abnormal haemoglobin compounds can be demonstrated by spectroscopic examination of the blood.

ii. Erythremia (polycythemia rubra vera).

This is a chronic disease characterized by an increase in the haemoglobin and red blood count of the blood. There is an associated erythroblastic activity of the bone marrow. Clinically there is a rather reddish cyanosis which is due mainly to the increased viscosity of the blood. This causes marked slowing of the peripheral blood circulation and an increased formation of reduced haemoglobin. Associated symptoms include lassitude, tinnitus, gastro-intestinal disturbances and an enlarged spleen. The presence of a persistent polycythemia without any demonstrable cause should enable a diagnosis to be made.

B. Cardiac Causes

i. Congenital heart disease—

Cyanosis is present in 30-40 per cent of cases of recognized congenital heart disease. When it occurs it may be due to one or more causes. Two of these causes are such that they allow poorly oxygenated blood to enter the arterial circulation. They are: (1) Pulmonary stenosis. This decreases the circulation in the lungs and so hinders adequate oxygenation. (2) Patent cardiac foramina. This allows venous blood to enter the left side of the heart and mix with the arterial blood.

In addition, some believe that after a time, myocardial weakness develops as a result of persistently poor blood supply to the heart.

The diagnosis is made on the history and physical examination. The essential facts are a history of cyanosis and poor exercise tolerance; physical examination usually reveals clubbing of the fingers and the presence of heart thrills and murmurs which are not those of rheumatic valvular lesions.

ii. Acquired heart disease—

Cyanosis in acquired heart disease is usually associated with other signs of myocardial failure such as dyspnoea, oedema, enlarged liver or basal rales. It may occur in failure from any cause.

The most important factor is decreased peripheral circulation due to a decrease in myocardial power and also to an increase in venuous pressure. There is also often a decrease in the degree of oxygenation in the lungs due to a co-existing pulmonary oedema. There is, then, less oxygen in the arterial blood and abnormally large amounts removed from it; the latter is the more important. The diagnosis should be made on the history suggesting heart disease and the signs of myocardial failure.

C. Respiratory Causes

i. Mountain sickness—Rapid ascent to considerable heights will cause a

variety of symptoms. These include cyanosis, headache, nausea, etc. Due to the decreased concentration of oxygen in the rarefied air, there is a decreased concentration in the alveoli and therefore, inadequate oxygenation of the blood. As a result tissue respiration can desaturate the blood to the threshhold for cyanosis.

ii. Obstruction—External or internal obstruction of the airways will cause cyanosis by decreasing the amount of oxygen which can enter the lungs. Here again inadequate oxygenation of the blood in the lungs is the primary factor.

History is important in diagnosis, especially a history of having had some object in the mouth.

iii. Emphysema—In this condition the oxygen saturation of the arterial blood may be considerably decreased. There are several reasons which are:

1. Decreased total aveolar surface.
2. Decreased chest movement and vital capacity.
3. Shallow breathing.

In addition to these factors which cause inadequate oxygenation there may be slower peripheral flow due to myocardial impairment.

iv. Pneumonia

Cyanosis is quite a common finding in pneumonia, being especially noticed in a widespread bronchopneumonia. In lobar pneumonia, involving one lobe or lung, little blood enters that lobe; most of the blood flows through the normal lung and is quite well oxygenated. In a spreading bronchopneumonia, however, lung function is diffusely and widely impaired. As a result, the total alveolar surface which is functioning is so much decreased that adequate oxygenation of the blood cannot occur. In addition the rapid shallow breathing in pneumonia is less effective in supplying oxygen to the alveoli.

For these reasons the blood which reaches the tissues is abnormally desaturated. After the normal gaseous exchange has occurred the oxygen desaturation has passed the threshhold for cyanosis.

The cyanosis and associated dyspnoea and anoxemia can be relieved by the administration of oxygen. While this does not directly change the course of the disease, it gives the body relief from anoxemia and saves a great deal of valuable energy. The diagnosis of the pneumonia provides the diagnosis of the cause of the cyanosis.

Summary

i. Cyanosis is a sign due to abnormal amount of reduced haemoglobin in the capillary circulation.
ii. It may be local, regional or general.
iii. It is associated with other signs and symptoms which will enable a diagnosis as to cause to be made.
iv. There are two main factors:
   A. Insufficient oxygen of haemoglobin in the lungs
   B. Excessive desaturation of haemoglobin by the tissues
v. There are three types of disease in which cyanosis occurs.
   A. Disorders of the blood or blood forming tissues
   B. Cardiac disease
   C. Respiratory disease
vi. The treatment of the primary disease is usually of first importance. However, if the chief factor is insufficient oxygenation, then the cyanosis can be relieved by the administration of oxygen, until the causative disease is cured.

The author expresses his thanks to Dr. Dauphinee for his advice and criticism.

ERYTHREMIA

By M. E. BORSOOK, '38.

Definition: For the purpose of limiting the scope of this paper, erythremia will be defined as an idiopathic absolute persisting polycythemia resulting from excessive erythroblastic activity of the bone marrow accompanied by a ruddy or cyanosed appearance and often with a palpably enlarged spleen. For this reason the pituitary or endocrine type will not be included.

Historical: In 1892 Vaquez reported a case with a peculiar cyanosis, an enlarged spleen with polycethemia, and suggested it was due to a primary hyperplasia of the bone marrow. His work was confirmed in 1894 by Widel and Rendu in France, Turck in Germany and in 1903 and 1904 by Osler.

Polycythemia vera is a medical curiosity because it is a conditon, in which, for a time, at least, we have too much of a good thing—namely, too many red corpuscles.

Age: It begins usually between the ages of 35-50 but may affect any age.

Sex: Both sexes are equally affected.

Race: Its highest incidence is among Eastern European Hebrews.

Incidence: There is a definite familial incidence. Some idea of its rarity may be gained from the fact that during the past ten years at the Toronto General Hospital there have been only eight cases. Because of this and the conflicting and often bizarre pictures presented by various cases, the etiology has been the centre of much interest and the subject of much controversy.

Etiology

The first important concept is that erythremia is the result of local anoxia of the bone marrow. This is the most recent view on the subject. Reznikoff and co-workers were impressed by a fact which had long been known that a large percentage of patients were Eastern European Hebrews. Hence, the disease was similar in racial and national incidence to Thromboangiitis Obliterans. Such a relationship seemed probable in that many erythremic patients complained of symptoms and exhibited signs referable to peripheral vascular occlusion and were treated for both conditions. Hence they felt that a study of the blood vessels of the bone marrow might yield valuable information. The following criteria were used by them to establish a diagnosis of polycythemia vera, which are the usual ones.

1. A polycythemia associated with splenomegaly which was distinct and persistent and which returned after a cessation of therapy.

2. The typical reddish cyanotic appearance of the patient.

3. Absence of any distinct lesion, such as occurs in pulmonary or cardiac disease which might explain the polycythemia.

They studied sixty-nine bone marrows, twelve of which were biopsy specimens distributed as follows:

7 from polycythemia vera cases —

62 from patients suffering various blood cyerasias.

The result of these studies showed that in all cases of erythremia there was a distinct thickening of the walls of the arterioles and subarteriolar blood vessels due to a marked fibrosis involving the subintima and adventitia. Some of the capillaries (where gaseous exchange occurs) showed an endarteritis obliterans. The blood vessels of the bone marrows of the 62 other cases uniformly failed to show these changes.

These findings suggest a line of investigation and merit further study in order to ascertain whether they will hold true for any large series of cases. They suggest the vascular changes particularly those of vessels of third degree may result in an anoxia of the bone marrow, which will stimulate a hyperplasia of the erythropoietic tissues re-

sulting in an excessive compensatory polycythemia.

Should these findings be confirmed, a firm physiological basis will have been established for one type of erythremia. Likewise with progressive vascular occlusion of the bone marrow vessels the terminal anaemia encountered in some cases is capable of logical explanation.

However the vascular changes which form the chief basis for this conception may prove to be secondary because of the marked tendency to degeneration of the blood vessels and of thrombosis in erythremia.

The second concept, which is the most widely held and probably will prove to be the correct explanation is that the disease is due to a primary hyperplasia, possibly malignant, of red cell forming elements of the bone marrow which is analagous and most likely allied to myelogenous leukemia.

There is ample evidence to support this point of view which will be stated briefly as follows:

(1) The great increase in the amount of red marrow which may be altered from the normal in character.

(2) The frequent occurence of extra-medullary haemopoiesis.

(3) The presence of abnormal and immature cells in the circulation.

(4) The increased amount of leucoblastic tissue and the latter's reflection in the peripheral blood by an increased white blood cell count and immature cells of the myeloid series.

The autopsy findings and some frank clinical cases supported strongly the hypothesis that erythremia bears a close relationship to myelogenous leukemia. The varying blood picture observed in these cases appeared to be a reflection of the degree of dominance of either erythroblastic or leucoblastic activity of the bone marrow.

Pathology

The bone marrow presents a characteristic picture. In gross it is typically red. Microscopically in addition to congestion, there is a hyperplasia of the erythroblastic and leucogenic tissues. Most of the signs and symptoms can be accounted for by the bone marrow findings. The spleen is always enlarged, even the Gaisback type when it is not palpable. This is due chiefly to vascular engorgement and to a lesser degree to hyperplasia of the pulp and in some cases to the presence of active haemopoietic foci. The latter may also occur in the liver, kidneys, lymph glands, in the perirenal and pelvic fat.

The blood vessels throughout the body are markedly injected because of the increased blood volume. The increased blood volume causes dilatation of the capillaries and eventually degenerative changes in the vascular system. Bleeding, cyanosis and stagnation occur. Because of the latter a vicious circle is established. The polycythemia impedes the circulation and the resulting stasis favours the development of cyanosis and increases the circulatory difficulty giving rise to a compensatory erythrocytosis in addition to the primary erythremia.

The increased blood volume which has been alluded to above can be demonstrated by the vital method of Keith Geraghty and Rowntree. An average finding is 125 cc. per kilo of body weight instead of the usual 85 c.c. This increase is almost entirely due to the increased number of the red blood cells and not due to an increase in blood fluid, a fact which can easily be demonstrated with the haematocrit. Normally the cells form approximately 47% of the total blood volume and the plasma 53%. In erythremia, the cells may occupy 73% of the total volume. Even without the haematocrit this fact can be demonstrated. If the blood is allowed to stand for a day almost no plasma comes to the surface. While the haemaglobin content of the blood is increased and not unusually reaches 150% of the normal as measured by the Haldane standard of 13.8 grams per 100 c.c., this is accompanied by a proportionately larger increase in the number of red blood cells. Consequently the colour index is distinctly less than un-

ity. Red blood counts varying from 7 to 11 million per cubic millimeter are not unusual. The white blood count is usually 15,000 or more. As the disease progresses the blood picture may change greatly and more closely resemble that of myelogenous leukemia with anaemia and a higher white cell count.

The red cells average 7 micra in diameter. An occasional normoblast may be found. Slight degrees of poikilocytosis anisocytosis and polychromasia are usual fiindings. There is an increase in the number of neutrophils. In some cases myelocytes and a marked shift to the left of the Schilling count are noteworthy findings.

The fragility of the red cells is somewhat abnormal. Haemolysis starts at .54% saline and is not complete in many cases until .06% is reached. Hence there is a marked increase in the resistance span. The normal resistance span is between .42% - 28%. This earlier onset of haemolysis accounts for the increased blood destruction which is reflected in a greater output in the urine and faeces of stercobilin and urobilin. This is not due to any overactivity of the reticulo-endothelial system. The normal stercobilin output in the faeces is between 60 - 100 mgms. Cases of erythremia have been reported with the output of 400 mgms. Hence the condition could not arise from decreased blood destruction.

The chemical characteristics of the blood are quite proportional to the increase in red blood cells. The total N.P.N. fat and uric acid is increased. The urine, when not complicated by renal hemorrhage may be normal or scanty. Albuminaria in varying degree is usually present. The sediment contains hyaline and granular casts. At times the urine is so abnormal as to suggest a co-existant nephritis which may be given further foundation by evidence of renal insufficiency as measured by kidney function tests with fixation of the specific gravity at a high level and retention of chlorides. However, these are usually transitory findings. With rest and proper diet these signs gradually disappear and kidney function returns to normal.

Physical Signs

On inspection the face, hands, feet, are usualy of a ruddy colour rather than cyanotic, although in the later stages pallor, because of anaemia may occur. Exposure to cold intensifies the reddish hue because of decreased local oxygen utilization while warmth causes an increase in the depth of cyanosis. On long-standing cases the skin becomes pigmented, and may be purplish. Teliangiectases and haemangiomata are common. The conjunctivae are notably blood-shot. The mucous membrane of the mouth and pharynx are deeply congested and blue. Superficial veins are prominent. Dependent oedema is usual, temperature is normal, the pulse slightly rapid and regular and of good quality. The heart may not be enlarged and the sounds are normal. The blood pressure in certain cases, particularly in the later phases is raised.

Papilloedema, haemorrhage and thrombosis of the retinal vessels occur. The spleen is always enlarged to a variable extent. In some cases (the so-called Gaisback type) it is not palpable. In others it may reach almost to the pubes, and may cause real distress. The liver is usually enlarged. The B.M.R. is increased and may be as high as plus 50%. This increase is proportional to the bone marrow activity. The total pulmonary ventilation is greatly increased and may reach as high as 14 litres per minute. Hence the arterial blood attains its normal degree of saturation and has an increased absolute amount of O_2. The need of the tissues for O_2 is not increased to any degree approaching the increased amount present in the arterial blood, hence the venous blood may be almost as rich in O_2 as normal arterial blood.

There is no marked increase in the minute output of the heart. Because the blood volume is so much increased the rate of flow lowered and the viscosity increased, the circulation on the whole is sluggish. Thus the tendency

to stasis which is a predisposing factor to thrombosis. Swelling of the large joints associated with the other cardinal signs of inflammation may suggest an infective arthritis.

Haemorrhage from the nose, gums, stomach and into the pleural and peritoneal cavities is not unusual. Cerebral haemorrhage is a common terminal event.

Unusual Symptoms

The onset is usually insidious and its exact date difficult to determine. Usually other members of the same family have a symptomless polycythemia for a long time. Often the abnormal colour of the skin brings the patient to the physician. Eye symptoms may be the first intimation of the disease. Blurring of vision, specks before the eyes, hemianopsia, transient blindness and dipoplia are common complaints. Tinnitus, vertigo, dizziness and headache are always prominent symptoms. Paresis, paralysis and paraesthesiae do occur. Then mentality may be abnormal, characterized by irritability and depression succeeded by euphoria. Speech embarrassment and amnesia are not uncommon.

There are frequent digestive symptoms, obstinate constipation, anorexia, a feeling of fulness, nausea and vomiting, unrelated to meals, cause much distress. Peptic ulcer occurs in 10% of cases. Thus the digestive symptoms may be of this condition.

Course

The disease pursues a chronic course lasting for years, characterized by remissions and exacerbations with progressive enlargement of the spleen and liver and a changing blood picture. While an intercurrent infection or vascular accident in a vital area may, at any time, terminate its course, frequently the disease passes into the anaemic phase characterized by a low red blood count, haemoglobin and colour index and a blood picture not unlike that of myelogenous leukemia. A similar blood picture may be presented during any phase of the disease. The anaemia which may eventually prove fatal may be explained in either of two ways:

1. Due to a crowding out of the erythropoietic tissues by the proliforating leucogenic tissues, or
2. The result of progressive occlusion of the bone marrow vessels.

Treatment

Therapy should be determined by the etiology and is directed in two directions (1) to remove the excess number of red cells from the circulation—or—to decrease their production.

Venesection is employed not only as an emergency measure but as a definite therapeutic adjunct. X-ray irradiation over the bones and spleen does decrease the rate of production of red blood cells and so far has proved the best means of control. This form of therapy should be discontinued when the red count is approximately 500,000 above the desired level as the decrease in the number of cells is delayed for a few days.

Phenylhydrazine or its less noxious derivative, acetylphenyl hydrazine are the haemolising agents used to destroy the red blood cells. Phenylhydrazine should be used with caution. The initial dosage is small and is gradually increased to avoid a haemolytic crisis. An initial haemolysis can be induced with 0.1 grams 2 or 3 times daily with the dose gradually being increased until a maximum dose of 0.4 grams daily is reached. This should be administered as long as the blood count continues to fall until the desired level is reached unless undesirable signs such as jaundice or gastro-intestinal upsets make their appearance. Its administration should always be controlled by frequent blood examination. When the red blood count has been reduced to between 5 - 6 million the condition may be kept under control by the administration of 0.2 grams three or four times weekly.

Radiation therapy would be contraindicated if a type of erythremia should

prove to be the result of vascular occlusion as it would merely hasten the onset of the anaemic phase. Therapy would then be solely confined to the use of venesection and haemolytic agents. However, the experience has been that roentgen radiation therapy is the most efficacious means of slowing the progression of the disease to its fatal termination as well as relieving any distressing symptoms that may occur.

Splenectomy is useless to allay the course of the disease but may be of great value by relieving the patient of a weighty mass which has been the cause of much distress.

The treatment of any disease is not complete unless the attitude of the patient to his illness is directed along lines conducive to the patient's happiness. This is particularly true of polycythemia vera with its long chronic course, and many distressing symptoms leading to a fatal termination. The patient should be encouraged to take an optimistic attitude. This can be honestly done, for with treatment, the patient can look forward to a varying period of years of comfort and moderate usefulness.

COUGH

By ALFRED BOCHNER, '38

Cough is a somewhat violent blowing out of the air-conducting tubes of the respiratory system.

How is this produced? First there is an instant of tight closure of the glottis by the laryngeal muscles. During this instant the muscles of forced expiration (abdominal muscles, latissimi dorsi, and lower part of trapezii) which exert their effect mainly on lower chest and false ribs, are brought into play, and by compression they instantaneously build up a high postive intrathoracic pressure. Then by sudden opening of the glottis a forcible outward blast of air is released. This can sweep out any loose particulate matter in its course.

The cough mechanism can be operated at will, as in announcing one's presence after entering a room too quietly. It also works reflexly in response to irritation of the bronchial mucous membrane. It is a natural protective mechanism.

The trachea and bronchi are lined by a ciliated epithelium in which goblet cells are numerous. The latters' secretion, augmented by that of numerous underlying seromucous glands, produces a fine bland protective coating for this delicate lining. The cilia are beating outward constantly to maintain a steady flow of this mucous coating away from respiratory tissue. With this flow, fine particulate matter, such as bacteria and various dusts, is carried off. The mechanism of outward beating cilia in mucous secretion extends as far down as bronchioles of approximately one millimetre in diameter.

In acute inflammation of the tracheobronchial mucous membrane by whatever agent, there first is a stage of congestion and swelling in which secretion is diminished. The consequent abnormal dryness and the congestion are irritating to local nerve endings, and impulses travel through the vagi to the special centres in the medulla which operate the cough mechanism. There is no secretion to be blown out, so this cough is without expectoration, and is called a dry cough, or a non-productive cough.

The stage of dryness soon gives way to one of abnormally abundant secretion and exudation, far more than the cilia can carry outward, so there is an accumulation in the larger bronchi, which exerts an unusual pressure on vagal sensory endings at the bronchial bifurcations, and the cough reflex goes into action to blow out the accumulated secretion and exudate. This is a

moist, or productive cough. Subjectively it is described as a loose cough. It is purposeful, and in so far as it removes its cause, is self-effacing. It is not apt to be distressing in itself, unless motivated by a very sticky secretion which is hard to blow out and therefore causes long spells of coughing. But coughing is a violent act, so that by the time such sticky secretion is dislodged and blown out, the oft-repeated violence may have produced congestion and irritation of the bronchial mucosa, which will continue to elicit the cough reflex after the cough's original purpose is abolished. This type of sticky secretion is produced by the more chronic inflammatory processes. The associated cough is dry or scantily productive. It is for the most part, not only purposeless, but self-perpetuating.

The purposeless cough is an agent for evil. It can cause sleeplessness, aching muscles in sides, back, and abdomen, exhaustion of an already weakened patient, and if continued for a long time, an emphysematous state of lungs and chest wall.

Where the cough reflex has gone wrong thus it can be hit on the head by the use of small doses of opium, morphine, heroin, and most commonly codein, any of which interferes with the reflex, probably on its sensory side, and so provides rest for the sufferer and a break in the vicious circle of a self-perpetuating cough.

In pursuing the subject of purposeless coughs it is noteworthy that the sensory side of the reflex arc is served by the vagus nerve. The vagi are distributed to ears, nose, pharynx, and stomach, as well as to larynx, trachea, bronchi, lungs, and pleura. Chronic dry cough can be produced by the irritation due to lesions in the foregoing extra-pulmonary sites, and such cough can be cured by treatment of the particular lesion.

Relevant to the cause of cough by stomach disturbance is the occurrence of nausea and vomiting due primarily to cough. When a patient complains of having vomited during or right after coughing spells one can, as a rule, presume that the coughing spells, from whatever cause, were very severe.

Chronic cough, without signs of disease in the chest, often is caused by some upper respiratory infection, such as chronic sinusitis or tonsillitis. Mucopurulent discharge from the nasopharynx or sinuses may drain down to cause cough only when the patient is holding his head up. If untreated, the continued dropping of infected material from an upper respiratory site may produce a bronchiectasis quite insidiously, and thus in time reverse the effect of posture in stimulating cough, or at least, the head-down position then would stimulate it too.

Another upper respiratory cause of cough, which is very common and is usually missed, is enlargement of the lingual tonsil (the lymphoid tissue at the base of the tongue). There are spells of most violent coughing, accentuated by laughter, hearty speech, or lying down. It tends to recur with each common cold. It is aggravated also by sudden changes in temperature, and by tobacco smoke. There is very little expectoration with it. There may be some substernal soreness to give the false impression of a tracheitis. Cough medicines apart from the morphine or codeine group have no effect on it. On pulling the tongue forward one can see the enlarged lingual tonsil with the aid of a throat-mirror. It acts here like a foreign body that cannot be expelled. The cure is performed by local application of a concentrated solution of ferric chloride, with care that none drops down into the larynx. The tonsil usually shrinks up sufficiently after a few applications.

An unusually long uvula may give a sense of tickling in the throat, and a cough habit may be established to combat this. Astringent gargles give relief.

Cough can be caused by a lesion in the larynx. It is generally dry and harsh, and associated with voice changes.

Croup is the term used to describe a peculiarly rough, barking or rasping cough. It is often associated with some difficulty in breathing and some hoarseness. There is the Membranous Croup of laryngeal diphtheria, and the spasmodic or simple croup of unknown etiology. The laryngeal diphtheria may be primary, or it may be secondary to diphtheria in nose and throat. Only in the latter will there be a two or three day precedent of illness with diphtheria as a clue. In the primary cases the course may be very insidious, and it may escape recognition until the onset of dyspnoea points to laryngeal obstruction.

The mechanical factors in croup are

1. Congestion of mucous membrane over the vocal cords.
2. Subglottic edema.
3. Diphtheritic membrane in larynx or trachea.
4. Spasm of laryngeal muscles due to local irritation.

The edema may occur in measles, retropharyngeal abscess, or quinsy, or in cases of obstruction by a foreign body.

The cough in acute and chronic tracheo-bronchial inflammation has been discussed already, with reference to the stages from harsh, dry and distressing cough to one that is productive and loose in the acute conditions, and a self-perpetuating dry or scantily productive cough in the chronic ones. Then there are the cases of copiously productive cough associated with such chronic bronchial lesions as those of bronchiectasis.

In bronchial asthma there may be a short dry cough at the onset of an attack, which passes off as the height of the attack is reached. With subsidence of the attack cough usually reappears and is first scantily productive of sticky sputum, and then of copious thin frothy sputum.

In the full-blown stage of whooping cough there are the absolutely characteristic whoops produced by inspiring forcibly through a glottis closed in spasm. The inspiratory muscles bear the brunt here. If the patient is very weak he may be unable to produce a whoop during the paroxysms of intense cyanosis and suffocation.

In pulmonary tuberculosis the cough may be a dry hacking thing when it first appears. The next striking event may be a pulmonary haemorrhage, or the patient may begin to find that by getting his head down low and coughing just as violently as he can for a while he can raise a small gob of rubbery sputum, and a sense of relief follows. With such very hard coughing there is produced vascular congestion in the head, and this may result in a little bleeding from the nose or throat which the patient believes is from his lungs. He becomes frightened and consults his physician, and in having this effect it is a good factor, although in about 80% of such cases there already will be something more than a minimal lesion. We cannot safely judge the extent of tuberculous pulmonary disease by whether the cough is dry or productive because that depends on the type of lesion as well as its extent. It is noteworthy that, in the current language of tuberculosis, a productive type of disease means one that is producing fibrous tissue, while the exudative type tends to produce destruction of pulmonary tissue and more copious sputum.

"It was a maxim with Foxey — our revered father, gentlemen — 'Always suspect everybody.'"

—*Dickens* (*Old Curiosity Shop.*)

Such an attitude of virulent suspicion, amounting almost to evil-mindedness, is essential for the early diagnosis of tuberculosis. Suspect everybody, and most certainly those who cough, and let it be an incentive to early diagnosis (probably not very early by this time). Yet one must be careful not to diagnose on suspicions alone, for the consequences of labelling a person as tuberculous are most serious and entail a revolutionary change in his mode of living for at least several years, as a rule.

The cardiac cough is a variable symptom. It is usually due to a mild bronchitis that has come from chronic congestion of the tracheo-bronchial mucosa. It is a short, dry or slightly productive cough, often occurring in spells on exertion. Cough may also be caused by edema fluid that has reached bronchial bifurcations. In acute edema there is the typical copious, frothy, pinkish sputum.

In most cases of frank pneumonia in adults cough is a prominent symptom. If there has been a preceding "cold," cough is present at the onset. If not, cough appears with or soon after the initial rigor, and is dry, often coming in spells. The associated pleurisy makes coughing very painful so that the patient attempts to suppress the cough, and this may add to his dyspnoea. In one to three days the cough may become productive and less distressing, or on the other hand it may become more severe and seriously tax the sufferer's strength.

In acute massive pulmonary collapse there is usually a slight cough from the onset, and the whole picture is easily confused with the foregoing if one overlooks the shift of the mediastinum and its contents (notably heart and trachea) to the collapsed side.

In lung abscess, dry hacking cough associated with pleuritic chest pain, some fever and malaise, and leucocytosis, may precede by several days the appearance of expectoration, and physical signs of intrapulmonary disease.

In pulmonary infarction cough usually develops soon after the event in the course of the first or second day. Possibly dry at first, it soon becomes productive of fresh bloody sputum, later rusty or brownish. If there is enough surrounding pulmonary edema there may be more copious, pinkish, frothy sputum.

In pulmonary new growths the cough is caused by irritation of the bronchial mucous membrane either by growth within the bronchus or pressure from without. It is almost a constant symptom but varies a lot in severity. Usually it is dry and hacking at first, often paroxysmal, particularly if there is obstruction within a bronchus. Later it becomes productive, and the presence of blood in the sputum is very common, especially when the bronchi are involved.

Other intrathoracic tumours when they press on bronchi or trachea, produce dry cough, which later becomes productive as a bronchitis develops at the site.

In aneurysm of the thoracic aorta cough may be produced similarly by pressure on the trachea. The cough may be peculiarly dry and harsh in character, otherwise described in the books as a "goose" cough, or a "brassy" cough, and we might presume that the latter association is with the band instrument rather than with an inarticulate lump of the gleaming metal. The brassy cough is mentioned by some authors in connection with pressure on the left recurrent laryngeal nerve as it traverses the aortic arch.

Uncommonly mitral stenosis has produced pressure on this nerve to cause paralysis of the left vocal cord, hoarseness and a brassy cough, and the diagnosis of aneurysm. Far more common in well-marked mitral stenosis is chronic cough and expectoration, blood-streaked occasionally, and a marked tendency to attacks of bronchitis with recurrence of bloody sputum. This is due to the pulmonary fibrosis (brown induration) in these cases. A pseudo-tuberculous picture is presented sometimes. Careful auscultation of the heart usually prevents such a mistake. It is logical to examine the heart before percussing the lungs.

Exposure to dust of any kind, even for a little while, often irritates the mucous membrane of the respiratory passages and results in cough (and sometimes sneeze). In the dusty trades usually the first thing noticed is frequent clearing of the throat due to a sense of mild irritation there. Later there may be a light cough coming only in the morning. With progress of the lesion there is more severe cough and

production of mucus. The inorganic dusts can produce progressive pathological changes in the lungs and bronchi, and, in time, disease and disability in the individual. Such disease can be prevented often. It occurs not only among gold miners (silica), but also for example among stone-masons (flint), potters (flint and clay,) workers in stone quarries (flint), metal grinders (silica), asbestos workers (asbestos), mirror-makers and glass-polishers (red oxide of iron).

Occasionally foreign bodies enter the air passages. After passing the glottis the object may lodge in the larynx or trachea. Most of these, however, pass down the trachea and of these about 80% enter the right bronchus. If it goes any further it is usually into the lower lobe branch. In any case there is produced irritation and spasm of larynx and trachea and more or less severe paroxysms of coughing in the attempt to blow out the object. If not successful the symptoms usually tend to subside as it lodges in one of the larger branches of the bronchial tree. If there is infection and a subsequent pneumonitis or tracheo-bronchitis, cough may recur in association with those conditions. 'A positive history of choking and gagging while eating peanuts or any food, followed by cough and wheezing is diagnostic of a foreign body having entered the trachea and bronchial tree . . . until proved otherwise.' (Norris and Landis, "Diseases of the Chest".)

There is still the cough of apparently nervous origin that has become just a habit, perhaps satisfying to some very shameful psychoneurotic demand.

There is also the fact that youngsters often cough without much fuss, and simply swallow their sputum, and we easily may miss the whole show.

Extremely violent coughing, as in whooping cough, can cause haemorrhage into the eyes, nosebleed, or cerebral haemorrhage, as well as herniation of abdominal organs, haemorrhoids, or involuntary micturition.

Whatever a cough has meant during its existence, its sudden disappearance may be of grave significance, portending the onset of coma or exhaustion.

In summary it may be stated that cough may be a symptom in the majority of the diseases of the chest, and in some diseases in areas served by the vagi nerves beyond the chest. As a symptom of disease it has a troublesome vagary of causes and conditioning factors.

The conclusion was stated by Laennec in 1818: "The diseases of the thoracic viscera are very numerous and diversified, and yet have almost all the same class of symptoms. Of these, the most common and prominent are cough, dyspnoea, and, in some, expectoration. These, of course, vary in different diseases; but their variations are by no means of that determinate kind which can enable us to consider them as certain indications of known variations in the diseases. The consequence is that the most skilful physician who trusts to the . . . . general symptoms is often deceived in regard to the most common and best known complaints of this cavity."

References.

1. Laennec: A Treatise on the Diseases of the Chest and on Mediate Auscultation. 1818.
2. Osler and McCrae: The Principles and Practice of Medicine. 1920.
3. Osborne, O. T.: The Evaluation of Symptoms. 1935.
4. Norris and Landis: Diseases of the Chest. 1931.
5. Kraetzer, A. F.: Procedure in Examination of the Lungs. 1935.
6. Meakins, J. C.: Practice of Medicine. 1936.
7. Bailey's Text-Book of Histology. 1932.
8. Hannah, B.: Lecture on Croup. 1937.

NEW METHODS OF TREATMENT FOR DEMENTIA PRAECOX

By S. D. CAMPBELL, '39

The average medical student regards the field of psychiatry as being a remote subject, one having very little implication for him. He thinks of mental disease in terms of the bizarre, and derives some amusement from the behaviour and appearance of patients suffering from this type of disease. Contributing to this attitude, perhaps, is the fact that until recent years there has been very little of a specific nature in the way of treatment. Up to the present all treatment has been of a general nature, consisting of fresh air, good food, exercise, occupational therapy and psychotherapy.

The science of psychiatry, however, *has* made tremendous advances in recent years in the field of diagnosis and prognosis. Treatment has lagged behind, but in the last three years great strides have been taken in the field of treatment, particularly of one form of insanity namely, Dementia Praecox.

Dementia praecox falls into that great sub-class of insanity called "the functional psychoses." It is a disease for which up to now, there has been no satisfactory treatment, explanation of etiology or real understanding of the psychopathology, other than careful objective description of the clinical picture. It constitutes the largest single institutional problem in Canada, since there are over 17,000 known cases. These patients require from one quarter to one third of all the occupied hospital beds in this country, and the disease accounts for more sick people than either tuberculosis or cancer.

This is not the place for a complete clinical description of the condition, but the main diagnostic criteria are as follows:

1. Dissociation of the cognitive processes, with blocking, and in severe cases, complete shattering of thought.
2. Disharmony between thought and affect (emotional life).
3. Certain disturbances in the perceptual field, such as hallucinations.
4. Frequent occurrence of delusions, usually of a bizarre nature.
5. Complete lack of insight.

As a rule the disease commences early in life, from 20 to 40 years of age, runs a progressive course without remission, until it terminates in a complete intellectual and emotional deterioration. The recovery rate has been very low, the most optimistic figures being about 12%.

When we realize the tremendous economic and social implications of this disease, which is in many respects a living death, the empirical and somewhat heroic methods of treatment recently developed are extremely interesting. On the basis of reported cases and partial cures, the results are much better than with any other form of treatment.

Insulin Shock Therapy—The method of treatment here is such as to require constant skilled supervision. The patient is given gradually increasing doses of insulin intra-muscularly, until a state of hypoglycemic coma is produced. This treatment is continued daily, with a rest period once a week, until the patient is free of symptoms, or until the treatments do him no further good.

Metrazol Convulsive Therapy—This treatment consists of the administration of certain drugs which cause irritation of the central nervous system to such a degree that convulsions occur. It was begun by V. Meduna of Budapest, and improved upon by Friedman in Buffalo.

The patient is placed on an alkaline diet, which is continued throughout the treatment. When this regime has continued for a week the patient is started on injections of prepared camphor. Two

injections are given intra-muscularly each day, with gradually increasing dosage, for 14 days. During this stage the patient must be closely watched for the occurrence of convulsions. The patient is then started on an intravenous injections of a 10% aqueous solution of Metrazol (penta methylene tetrazol). The dose given is sufficient to produce a convulsion, usually 6-7 cc. Within 30 seconds of the injection there is produced a typical grand mal epileptic convulsion, and the complete reaction is usually over within 30 minutes. The treatment is continued until the patient has had 20 to 30 convulsions, and is terminated depending upon the clinical response of the patient.

In the selection of suitable cases the criteria are the same for both types of treatment, namely, a certain diagnosis, physical condition, and duration of illness.

The figures for the results vary but at present 80 to 90% show recovery or apparent recovery in cases where the disease has had a duration of less than 6 months. As the duration of the disease rises the recovery rate falls off.

Following the course of treatment the patient is given superficial, supportive psychotherapy, is placed in a suitable home and is able to go to work 2 to 3 weeks after the completion of the treatment.

This treatment, although it seems very drastic, is interesting in the light of its success in early cases. Canadian psychiatrists are watching with conservative interest the results of the experimental treatments, and in most provinces experimental wards have been established for the study of the treatment. While it is yet too early to assess the true value of this form of treatment, the results seem to justify further investigation of the reasons for the remarkably high remission rate.

At present the reasons are obscure. Some believe that such a shock to the whole system literally shocks the patient out of his psychotic state. Others think that the anoxemia of the brain found in insulin shock, and the similar anoxemia produced by contraction of the cerebral arterioles, in the Metrazol convulsions, plays the important role. The relation of the anoxemia to the mental processes, and psychotic states has not been determined, and the problem remains one which will have to be solved in the future.

The writer is indebted to Dr. C. M. Hincks and Dr. J. D. Griffin for suggestions and material for the preparation of this paper.

LEADING MEDICAL TEXTBOOKS

Arey's Developmental Anatomy.
Beckman's Treatment.
Boyd's Pathology of Internal Diseases.
Boyd's Surgical Pathology.
Boyd's Textbook of Pathology.
Brown & Tisdall's Common Procedures in the Practice of Paediatrics.
Cecil's Medicine.
Christopher's Minor Surgery.
Christopher's Textbook of Surgery.
Cunningham's Manuals Practical Anatomy.
Cunningham's Textbook of Anatomy.
Curtis' Textbook of Gynaecology.
DeLee's Textbook of Obstetrics.
Dorland's Illustrated Medical Dictionary.
Grant's A Method of Anatomy.
Griffith & Mitchell's Pediatrics.
Henderson & Gillespie's Psychiatry.
Hutchison & Hunter's Clinical Methods.
Jordan's General Bacteriology.
Maximow & Bloom's Histology.
Meakins' Medicine.
Norris & Landis' Diseases of the Chest.
Ranson's Anatomy of the Nervous System.
Schumann's Textbook of Obstetrics.
Sollmann's Pharmacology.
Todd & Sanford's Laboratory Diagnosis.
Treves & Choyce's Surgical Applied Anatomy.
Wright's Physiology.

McAinsh & Co. Limited
Dealers in Good Books Since 1885
388 YONGE ST. TORONTO

TISSUE OXIDATION

By PAUL GREENBERG, B.A., '40.

Many compounds are utilized by the body for the production of energy, and for the formation of different chemical substances. Most of these utilizable compounds are stable in the presence of molecular oxygen, and therefore are not ordinarily oxidized in air. The question arises: how are these substances oxidized in the body? The fact that they are oxidized is supported by an overwhelming amount of data. It is now known that this oxidation is catalyzed by enzymes, and so ultimately the mystery of tissue oxidation is linked with the enigma of the enzyme.

Oxidation.

A substance may be oxidized in two ways. It may lose hydrogen, as when an alcohol is oxidized to the corresponding aldehyde, or it may gain oxygen as when an aldehyde is oxidized to the corresponding acid. There can also be oxidation in which the gain or loss of oxygen or hydrogen does not necessarily occur. This is exemplified by the oxidation of a ferrous compound to a ferric compound. In this case the ferrous atom is oxidized by the loss of an electron. Reduction occurs when the atom gains an electron. In any case where there is oxidation there must be simultaneous reduction.

Methods of Oxidation.

The study of tissue oxidation may be said to have begun with Schönbein in the middle of the last century. He, the discoverer of ozone, believed that the essential reaction was one in which oxygen was "activated" and that this active oxygen reacted with the substrate, the substrate being oxidized. This view was held because in the investigations undertaken at that time the oxidizing systems were active only in the presence of oxygen or peroxides.

Bach and Engler were led to the belief that oxygen from the blood reacted with some protoplasmic constituent to form a peroxide and that this peroxide was broken down yielding active oxygen.

Warburg also believes that the activation of oxygen is the essential factor. He believes that this activation occurs through an iron compound which he calls "das Atmungsferment." According to him oxygen combines with this compound, and the resulting substance in turn oxidizes organic substrates.

A controversy arose between Warburg's school of thought and that of Wieland and Thunberg. These later workers showed that tissue oxidation can progress in the complete absence of oxygen or peroxides. They expressed the belief that tissue oxidation is due to the removal of hydrogen from the substrates. The enzymes so involved are called "dehydrogenases." This controversy was resolved somewhat by Keilin, who demonstrated the cytochrome system. Both methods of oxidation are involved in that system.

Cytochrome System.

According to Keilin, cytochrome is oxidized by Warburg's Atmungsferment, an enzyme which is believed to be identical with that which catalyzes the oxidation of dimethyl-paraphenylene diamine-hydrochloride and a-naphthol to indophenol blue; and which is known as indophenol oxidase. The oxidized cytochrome then becomes reduced through the agency of hydrogen removed from cell metabolites under the action of dehydrogenases.

Das Atmungsferment (Respiration Enzyme).

By means of this substance cytochrome is oxidized. The enzyme is oxidized directly by oxygen and is an

iron compound; its activity is inhibited by cyanides.

Cytochrome.

Cytochrome is an iron pigment which is found only in aerobic organisms. It consists of three components, all believed to be haemochromogens, and known as cytochrome a, cytochrome b, and cytochrome c. These are believed to have a common protein base and contain iron in a porphyrin nucleus. Each of these components in the reduced state has a distinctive absorption spectrum. This has been used to demonstrate the action of cytochrome in the moth and in suspensions of yeast cells. The absorption spectrum is observed under normal conditions. The oxidation of cytochrome is prevented then, by adding cyanide to the suspension of the yeast. (Or in the case of the moth, by causing it to perform strenuous exercise, a temporary anoxia prevents the full oxidation of the cytochrome). The absorption bands then appear. On oxidation of the cytochrome the absorption bands become very indistinct. The respiration enzyme is necessary for the oxidation of cytochromes a and c, but not for cytochrome b. This latter component is auto-oxidizable. According to the Warburg-Keilin view, oxidation is brought about thus: the oxidized Atmungsferment oxidizes the iron in one of the cytochromes to the ferric state, being reduced itself, of course. This ferric iron oxidizes the ferrous iron in the next cytochrome component, and this in turn oxidizes the iron in the third component. The third component of the cytochrome system is reduced by the dehydrogenases.

Dehydrogenases.

These are enzymes that catalyze the removal of hydrogen from the substrates. There are two groups of dehydrogenases:

(1) *Aerobic.* These enzymes (for example the dehydrogenase responsible for the oxidation of xanthines), can transport hydrogen directly to oxygen. That is, oxygen acts as the hydrogen acceptor with aerobic dehydrogenases.

(2) *Anaerobic.* This type cannot transport hydrogen directly to oxygen, but requires an intermediate substance. For example, if methylene blue is present the hydrogen is donated to that substance, which is thereby reduced. Molecular oxygen oxidizes this reduced methylene blue. Thus in the presence of oxygen the substrate can be oxidized if methylene blue is present. There is no oxidation if methylene blue or a substance with a similar action is not present. Cytochrome plus "das Atmungsferment" acts in the same way as the methylene blue. Dehydrogenases are specific for the substance that is oxidized but frequently are not specific for the substance that is reduced. Narcotics inhibit their action.

The cytochrome system probably accounts for ten per cent. of the oxidations in average tissues. In some aerobic bacteria, oxidation has been shown to proceed almost completely by the cytochrome route.

Peroxidase and Catalase.

When molecular oxygen acts as an hydrogen acceptor, hydrogen peroxide is formed. Catalase acts specifically on this substance, breaking it down to water and molecular oxygen. The catalase protects the cell from the action of hydrogen peroxide, which is very toxic to enzymes. Catalase is a hemin compound and is inhibited by cyanides. Peroxidases catalyze the breakdown of hydrogen peroxide and organic peroxides, especially phenolic peroxides. Active oxygen is liberated which can oxidize some non-specific substrate.

Flavin System.

The flavins are pigments which have a wide distribution. They may occur free or bound to protein. One of these occurs in the "yellow enzyme" which has been isolated from yeast, and which consists of protein, phosphoric acid, and the flavin which is identical

with the growth factor in vitamin B_2. It has been synthesized.

The flavin system is completed by colloidal substances, called by Warburg "zwischenferment," and by a coenzyme which has turned out to be adenine-b-nicotinamide-3-phospho-2-ribose. Oxidation is accomplished as follows: Two atoms of hydrogen are transfered from the substrate to the coenzyme under the influence of the zwischenferment (probably a dehydrogenase). The hydrogen is then transferred from the coenzyme to the yellow enzyme and from here to molecular oxygen, forming hydrogen peroxide. Intervening between molecular oxygen and the substrate undergoing oxidation there are, therefore, *two* reversibly oxidizable substances, namely the coenzyme and the flavin enzyme.

Glutathione and Vitamin C.

Glutathione by virtue of its sulphur group can be alternately oxidized and reduced. This can be represented thus:

GSH==GS-SG (oxidized).

Most of the substances and systems which oxidize and reduce glutathione are not fully understood. It is thought by some investigators, however, that vitamin C is the most important oxidizer.

Ascorbic acid (vitamin C) can also be alternately oxidized and reduced. Oxidation is catalyzed by an enzyme, ascorbic acid oxidase. Glutathione and ascorbic acid apparently work together in the tissues:—catalyzed by the ascorbic acid oxidase, ascorbic acid is oxidized, this then oxidizes glutathione, which in turn oxidizes some tissue substrate or substrates, perhaps with the assistance of dehydrogenating enzymes.

Of the systems concerned in tissue oxidation which have been investigated up to the present time, the main ones have been briefly described. There have been other systems suggested, such as the dialuric acid-alloxam system, but the importance of these has not been demonstrated. Other oxidizing enzymes occur, such as tyrosinase (not demonstrated in mammalian tissues), dopa oxidase, and others.

The cells rely on oxidation for their activity, and for their very life, and therefore on the systems that make this oxidation possible. Very fertile fields of speculation are apparent, the tilling of which will probably yield interesting results. For example the impairment of some of the mechanisms of oxidation must lead to pathological changes in the cells affected. This has been demonstrated in the brain in avitaminosis B_1. The Flavin system may be involved in Addison's disease, in which phosphorylation of the flavin seems to fail. Further study along similar lines might throw much light on other pathological conditions whose etiology is as yet obscure.

The author wishes to express his thanks to Dr. Wynne of the Department of Biochemistry for his aid and criticism in preparing this paper.

The Gayest Shop in town . . .

Rendezvous of smart shoppers who want the latest—the Continental Shop is now gay with practical gift suggestions for Christmas.

A gift sent from here has that desirable originality at $2 or $20.

Reasonably priced, the gifts you choose here will reflect your knowledge of what is new and original.

BIRKS - ELLIS - RYRIE

Yonge at Temperance » » TORONTO

Medical Society Notes

By W. K. KERR

The second year executive, with Mr. Gain as president, is to be congratulated upon the success of the Soph-Frosh dance on November 5th. Everybody from the patrons to those of the first year students who were there, enjoyed themselves. But the great number of first and second year students who were not there that night is a source of concern to the Medical Society. From various sources it has been suggested that the dance be an informal one; no doubt this would ensure a greater patronage of those from whom the dance derives its name. The idea must be passed on to next year's executive for consideration.

It is a pleasure to note that the Frosh have already brought laurels to our faculty. They came out victorious in the chariot race, Meds. vs. S.P.S. during the intermission of the McGill-Varsity game. We should like to pay tribute to the Ben Hur of that day; but several telephone calls failed to reveal his identity.

The Medical Society has been approached by several organizations wishing the Society to send delegates or contribute money toward the expenses of delegates to their conferences. The National Student Conference is one instance. The Medical Society is sensibly aware of the importance of bringing together students from different universities for discussion of problems social, political, national and religious. To arouse an interest in the social development and political leadership of our country among university students, the future intellectual elite of that country, is admittedly a cause worthy of encouragement. And yet, the funds under the administration of the Medical Society, accrued as they are from fees of the medical students, should be expended firstly in the interests of those students. According to an amendment of the constitution of the Medical Society of which a majority of the students were in favour at the spring elections, 1935, all available funds of the Medical Society are to be turned over to the Board of Governors for the purpose of lending financial support to needy and worthy Medical Students. At present this bursary fund, though generously augmented by the Board of Governors, is not nearly adequate to take care of all those students deserving of help.

Therefore, it is still the opinion of all members of the Medical Society that unnecessary expenses be curtailed to a minimum in the interests of the student body. This expression of policy explains why the Society cannot contribute money towards the sending of delegates to the Winnipeg Conference.

Attractive Prices
Convenient Location
Browse at Will
Service

• • •

The New Management of
The University of Toronto Press

• •

Is Very Anxious That You
Make Yourself at Home
In Your Own University
Book Store

•

Medical Athletics

By W. B. CHARLES

The end of the interfaculty rugby schedule finds neither of the medical teams very far up in the standing. Nevertheless they gave a good account of themselves in every game and enthusiasm was maintained until the last. A great deal of credit is due to the managers of these two teams for their willingness in giving of their time and efforts and for the efficient manner in which they carried out their duties.

A great many medical students are, perhaps, not aware that there is such a thing as a medical soccer team. Well, there is and this year it is a very good one. They have not lost a game during the regular schedule and at the time of writing there is a possibility that they will draw a bye into the finals for the university championships. When the team won their first game of the season it was the first soccer victory for Medicine in two years so that the good showing of the team this year is a welcome addition to the record of Meds in interfaculty sport.

There are a great many medical students who play squash regularly. Up to the present any attempts to hold a tournament for them have not met with very much success. At the time of writing there is a tournament in progress which it is hoped will be the first of an annual series, and in order to place this event on a firm basis a suitable award is to be made to the winners, beginning this year. The nature of this award will be announced in the near future.

It is with a great deal of pleasure that we officially announce the formation of the Medical Indoor Track Club. This is an activity that has been very much neglected of late in this faculty and we sincerely hope that this will lead to revival of interest among medical students in track and field. The Medical Athletic Association had nothing to do with formation of this club and all credit is due to the group of students who conceived the idea and carried it out and we congratulate them for their enthusiasm and wish them every success in the meets at Hart House this winter. The Athletic Association will assist this new club in any way it possibly can. For information regarding the club and its activities refer to H. M. Schlachter, third year.

The latest available figures show that Medicine ranks sixth in the intramural competition for the T. A. Reed trophy. The year is yet young and Meds will no doubt find their way closer to the top as more of the schedules are completed. This faculty ranked third among all faculties when the final standings were announced last spring—a very creditable performance indeed and one which will keep us hard pressed to surpass this year.

When this is read you will probably have noticed the boards which have been put up—one in the medical building and one in the T.G.H. cloakroom. In future all athletic notices will be posted on these boards and it is hoped that they will assist the students in following the activities of the various teams.

Feature Section

ON THE DANGER OF SCRAPPINESS

By Professor William Boyd, M.D.

Our fathers and grandfathers were brought up to appreciate the value of thoroughness. We admire it in them and in their writings. The Victorians knew their reading, writing and arithmetic. But it was much easier for them than for us. The conditions of modern life make for diffuseness and scrappiness. There is a modern craze for news. Not only are there newspapers, or rather sheets of advertisements amongst which snippets of information are scattered here and there, but there are weekly newsmagazines containing so much information that by the time you have finished one issue the next is arriving, and picture magazines with news, hot or otherwise, whilst the radio in the intervals of crooning gives us news from all parts of the world.

Now news is one of the most interesting of things. The newspaper man calls it a story, and he is right. But it has its dangers. You may remember that when Paul came to Athens he found that the people were always seeking after some new thing. Yes, but that was after the Golden Age had passed away. News is delightful for the old, for the business man who has nothing to do with his evenings, for the feeble minded. But for the student it is a seducer whose danger is its apparent innocence. It fills the mind with scraps of information, but the student's aim and ideal should be thoroughness, not scrappiness. It is thoroughness which makes a man a great golfer or figure skater, a great internist or anatomist. But thoroughness and distraction do not go together. I have seen a man studying (?) in a room in which the radio was playing! Such men always feel aggrieved when the list of supplementals comes out.

Another cause of modern scrappiness of mind is the "digest habit." On every bookstall you will see a digest of this and a digest of that, handy little magazines which can be slipped into a pocket or carried on a street car. In these places they are splendid, and they will enable you to produce scraps of literary information at a dinner party like a conjurer produces rabbits from a hat. But they have no place in a student's study. His time and the integrity of his mind are too precious. For they do not take the place of the books they abstract. Recently I read a "digest" of "An American Doctor's Odyssey," and afterwards I read the book itself. The impression created on my mind was absolutely different in the two cases. Imagine reading a digest of King Lear or the Forsyte Saga or The Seven Pillars of Wisdom. Besides, if you are always taking things predigested, what is going to happen to your own digestive organs?

May I suggest to the students of our medical school that great pleasure and satisfaction is to be derived from knowing one thing really well, from being master of one subject however small. Thoroughness rather than scrappiness. And with that thoroughness will come competence and mastery, and such mastery will bring the recognition from his fellows which every man enjoys. As Emerson says: "Let a man preach a better sermon, write a better book, or build a better mouse trap than his neighbour — though he build his house in the woods, the world will make a path to his door."

A thorough knowledge of a subject is possible in two branches of thought, the one professional, the other general. The medical student may set himself to become an expert on the anatomy, histology, and physiology of an organ, or on the pathology and clinical features

of a disease. The former is more likely to appeal to him in his earlier years, the latter in the clinical part of his course. Should a man interest himself in such an organ as the kidney, prostate or parathyroid, he will be surprised how frequently new information regarding his pet subject meets his eye. The "news" may be scrappy, but it will be integrated in the mind so as to form part of a composite whole. The same is true of a disease such as coronary occlusion, cholecystitis, or bronchogenic carcinoma.

In the field of general reading a student may also become an expert. It is remarkable how in a very few years one can read all the works of an author that are worth reading, and when the author is a master of matter or style, these insensibly colour the mind of the reader. But such reading can only be done if one is aware of the danger of scrappiness. "Paradise Lost" and "The Ring and the Book" may appear alarming because of their length, but in my third year in medicine at Edinburgh I read the twelve books of Milton's immortal work on Sunday afternoons before Christmas and the twelve books of Browning after Christmas.

Each man has to decide for himself what he wants, but there is not time in the study of medicine to colour the mind with Robert Louis Stevenson or Conrad as well as the latest gossip from Hollywood. "Do you know" says Ruskin, "if you read this, that you cannot read that — that what you lose today you cannot gain tomorrow? Will you go and gossip with your housemaid or your stableboy, when you may talk with queens and kings, or flatter yourself that it is with any worthy consciousness of your own claims to respect that you jostle with the hungry and common crowd for entrée here and audience there, when all the while this eternal court is open to you, with its society wide as the world, multitudinous as its days, the chosen and the mighty of every place and time?"

Great books are the greatest relaxation that the world can offer to the hard worked medical man, be he student or practitioner. In his brief moments of leisure he can turn to the great silent company who stand on his bookshelves waiting to be heard. "For a man's true life for which he consents to live may lie altogether in the field of fancy. The clergyman, in his spare hours, may be winning battles, the farmer sailing ships, the banker, reaping triumph in the arts; all leading another life, plying another trade from that they chose. For to look at the man is but to court deception. We shall see the trunk from which he draws his nourishment; but he himself is above and abroad in the green dome of foliage, hummed through by winds and nested in by nightingales. For no man lives in the external truth, among salts and acids, but in the warm phantasmagoric chamber of his brain, with the painted windows and the storied walls."

If you know your Robert Louis Stevenson you will know where that comes from, as well as dozens of other passages which will become part and parcel of your mind. But such knowledge will never come if you abandon yourself to scrappiness.

EXPERIMENTAL CANCER RESEARCH

On Wednesday, November the third, the students of Sixth Year and a large number of the teaching staff had the privilege of listening to a lecture on Cancer Research given by Dr. Gye, the Director of the Imperial Cancer Research Fund. The lecture was a masterpiece of clearness and was presented in a delightful manner. Your editor took notes as carefully as possible and was so impressed by the fascinating nature of the material presented that he decided to attempt to reproduce the lecture for the benefit of the readers of this journal. Apologies are offered to Dr. Gye for any mistakes or misinterpretations of his lecture as printed below:

As a basic concept in the appreciа-

tion of the cancer problem, one must understand that cancer is essentially a disease of the individual cell. It was believed until early in this century that cancer occurred only in the human. In 1903, however, Bashford examined carefully a large number of mice and found mammary cancer in 6% of these animals. Subsequently, he demonstrated that the condition could be found in all vertebrate animals if looked for. His next step was to accomplish successfully the transplantation of mammary carcinoma in mice. In these transplants it was apparent that the stroma of the transplanted tissue died and was replaced by stroma from the host while the actual carcinoma cells lived and multiplied in the host unchanged in their character by the change in environment. It is thus an actual fact that the tumour cells growing in mice to-day are lineal descendants of the cells of the original transplant. It is apparent, as stated above, that cancer is a disease of the individual cells which originate the tumour.

With this concept established it appeared that an attack on the problem of cancer could be best carried out by a careful investigation of these diseased cells. What was there about them which would explain their property of autonomous growth? The earliest investigators attempted by devious methods to obtain some organism from these cells. None was found. Moreover, it was shown that if the cell was killed by any method whatsoever, successful transplantation of tumours could not be accomplished. The property of malignancy was apparently not dependent on any substance or organism within the cell but rather was due to some mysterious change in the constitution and metabolism of the living cell. Laborious investigations were then undertaken to discover the nature of this change. The ratio of nucleus to cytoplasm, the arrangement of chromosomes, the nature of the biochemical processes going on within the cell, were all studied. The result was entirely negative. Nothing within the cell could be found to account for the property of malignancy. The problem appeared insoluble.

Before further progress could be made, it was necessary to revise the concept of the etiology of cancer. It was necessary to divide the etiology into two separate divisions. Borell pointed out that when a cancer is transplanted from one animal to another we take a cell *already cancerized.* Many antecedent changes must have occurred to transform a normal cell into the malignant cell. Many forces have acted to produce that change. These factors may be called the "Remote Causes" of cancer. Now it is also necessary to explain the autonomous nature of the cell once it has become cancerized. The factors responsible for this are called the "Intimate Causes" of cancer. Before the Great War nearly all research was directed towards an elucidation of the proximate causes. Since the War almost all the work has been interested in the remote causes. Obviously, to fully understand the problem one must consider both causes.

In regard to remote causes, it was Percival Pott who in 1775 first demonstrated the association between soot and epithelioma of the scrotum in chimney sweeps. Not, however, until 1917 was experimental demonstration of the production of cancer by irritation carried out successfully. In that year Yamigiva showed the development of epitheliomas on rabbits' ears which had been painted with coal tar for two to three years. This was an outstanding contribution to cancer research. Kennaway and Cook immediately began the search for the carcinogenic constituent of coal tar. They soon discovered a whole host of pure hydrocarbons which were definitely carcinogenic. And to their delight and amazement it occurred that every one of these substances contained the phenanthrene nucleus. It seemed quite apparent that this radicle was the cause of cancer. The question seemed to be settled beyond all doubt when the eager chemist showed that many natural products of the

human body contained this nucleus, Cholesterol, ergosterol, 3. 4, benzpyrene and oestrin all fell into this group. And methylcholanthrene which was obtained from bile salts by a very simple chemical reaction, was an extremely active carcinogenic substance. Surely the solution of the cancer problem was at hand. It was disturbing, however, that further investigation revealed other substances which were carcinogenic and yet had no relation whatever to phenanthrene. Aminoazo-toluene when fed to rats gave carcinoma of the liver. A complex compound 3, 4, 5, 6, dibenzcarbazole when painted on the skin gave carcinoma. And a substance used to cure trypanosomiasis in mice produced carcinoma in the animals so treated. But none of these substances bore any simple chemical relationship to phenanthrene. The problem was not as simple as it had formerly appeared.

An advance was made, however, when it was shown that oestrin would produce cancer under special conditions. To understand this one must recall the influence of heredity in cancer. Murray in 1917, showed that by inbreeding mice showing mammary carcinoma. he could produce a strain which was highly susceptible to this condition. a so-called "High Cancer line." 90% of the females in this line would, if left alone, develop cancer of the breast. But if these females were taken when very young and their ovaries removed only 10% of the animals developed cancer. This was confirmed by other workers who excised the ovaries even earlier and obtained only 1% of cancers. Now ovaries were taken from females of this "High Cancer line" and transplanted into male mice of the same strain where they grew fairly well. One can imagine the amazement of the investigators when cancer of the breast developed in these male mice when such a condition had been previously unknown in male animals. Now Laccasagne showed that chemically pure oestrin injected under the skin of the males of the "High Cancer line" induced the development of carcinoma of the breast.

Bittner and Little then took newborn mice of the "High Cancer line," which would normally develop cancer in 90% of cases and fostered them on mothers from a "Low Cancer line" in which cancer only developed in 1% of animals. The result was astounding. Only 15% of the babies developed cancer of the breast. The reverse experiment was immediately carried out. Newborn babies of the "Low Cancer line" were fostered on mothers of the "High Cancer line" and behold 20% of these babies developed mammary carcinoma. There was no escaping the fact that something in the milk was a factor in producing or inhibiting cancer. The mystery of cancer was becoming still more mysterious.

Now Little took fertilized tubal ova from mice of the "High Cancer line" and placed them in the uteri of the "Low Cancer line" mice. One hundred and fifty female mice were produced in this way and *not one of them developed cancer*. From which is drawn the inescapable conclusion that genetics per se have nothing to do with cancer. It is something from the mother's body which is responsible for the development of cancer susceptibility in the offspring!

It is apparent at this point that although considerable light has been shed upon the remote causes of cancer, nothing whatever is yet known about the proximate causes. What property *within the cancer cell* allows it to go on reproducing itself in complete disregard of the rest of the body tissues? The beginning of a solution came in 1910 when Peyton Rous discovered a spindle-celled sarcoma in chickens. From this he obtained a *cell-free filtrate* which on inoculation into another chicken produced an exactly similar tumour. This seemed so heretical in comparison to the former views of cancer that it was disbelieved and disregarded by other workers for many years. But Rous continued his work. He discovered an osteochondrosarcoma which could be similarly transmitted. And these agents could cause only the type of tumour from which they were obtained! It was a miracle. Since

then Rous has discovered some two hundred such tumours of various kinds. His facts are incontrovertible.

The carcinogenic substance in these extracts is very labile. It cannot be cultivated outside the living body. It is destroyed by heat and is susceptible to oxidation. It can be centrifuged out of the filtrate and is then found to be composed of very tiny round particles all the same size. It is, in brief, *a virus*. It produces a tumour and increases pari passu with this tumour. Now note the difference between this and the previously discovered carcinogenic substances. The latter can cause a cancer to develop but they cannot be obtained from the tumour. Their job is done when the tumour starts to develop. They belong to the group of remote causes. The virus is the proximate cause. One is justified in considering that if all the virus could be extracted from the tumour by some powerful magnet, then the tumour would cease to grow.

There was, as stated above, great hostility to this notion. This was probably because of the ingrained idea that cancer is not an infectious disease. This is, of course, true, at least in a sense. But the parasite-host idea is not as simple as it is usually considered. Infection does not always occur when the organism enters the tissues of the host. This can be illustrated by considering tetanus. The spores of this organism are usually quite harmless to tissues which they may enter. They may be injected into mice and will cause no lesion or disease whatever even after many months. But let some calcium chloride be injected at some subsequent time, say six months later, and a rapidly fatal case of tetanus develops at once. It is apparent that certain organisms are only infectious under certain very particular conditions. One can imagine the cancer virus behaving in this way. It does not take effect until the conditions are just right.

The final step in establishing this theory was to demonstrate the role of virus in producing cancer in mammals. Tar was applied to the skin of rabbits for three months. (It usually takes about three years to produce cancer in this way). Then there was injected intravenously into the animal a cell free extract from a previously produced tar cancer. Forty days later the area painted with tar became intensely malignant and the rabbit died rapidly of extensive carcinomatosis. It seems apparent that the tar prepares the soil and if a suitable virus comes along, cancer develops. The tar injures the intracellular defense mechanism against cancer virus. Generalizing, one might say that two factors are necessary to produce cancer:

1. Something to prepare the tissues for the invasion of the virus.
2. The cancer virus to confer the property of autonomous growth on the cells which it is able to invade.

CANADIAN
LABORATORY
SUPPLIES
LIMITED

Canada's Leading Laboratory Supply House.

Headquarters in Canada for
LABORATORY APPARATUS
AND CHEMICAL REAGENTS

MONTREAL, QUE.
296 St. Paul St. West.

TORONTO-5, ONT.
Hartz Building. 32 Grenville Street

POST-GRADUATE WORK IN ENGLAND.

In reply to a request from the editor, a recent graduate of this school who is at present in England, wrote as follows regarding opportunities for, and expenses of, post-graduate work in England.

"To come here one needs about one hundred and fifty dollars, that is for boat fare and about two weeks hotel expenses. One should always come early in July as there are any amount of 'locums' going at that time. Hospitals pay from six to seven pounds a week. General practice pays eight pounds, supplies a car and all expenses. You can *always* get a locum of some sort here if you are hard up. In the summer months you can choose your own locum. In the winter, you more or less have to cast about for them.

Now as to hospital appointments: It is almost impossible without influence to obtain an internship in the big London teaching hospitals. In the provinces they are easy to obtain, if you have a year or two in hospitals at home. They pay on an average about one hundred and fifty pounds a year.

The advantage of the above is this. I know two chaps who went home after eleven months here with two hundred pounds in their pockets. Now this spread over another year would cover easily about six months' intensive study in London. It costs about two pounds, ten shillings a week for decent living accommodation and of course the fees vary greatly.

Practice here is much different than at home. First of all the right thing to do is to take an assistantship. These may be obtained easily but one must always be careful to pick a good one. The idea is always to take one with a view to partnership. Otherwise, you just do the work for a set salary which runs about four hundred to four hundred and fifty pounds a year. A partnership is bought. You pay about two thousand pounds for a share bringing in fifteen hundred pounds. This money can be borrowed from loan companies for doctors. It works out at about ten per cent. interest over ten years. Often, however, the senior partner will take so much from your yearly earnings and this is much more satisfactory. Of course any partner increases a practice so that your share becomes more valuable. It is saleable at any time.

Practising medicine here, as I have been doing for seven months, is quite pleasant. Although 'time off' is not very great, the work is not too strenuous. I am sure most Canadian physicians work harder.

I hope this has given you some idea of the 'pounds, shilling and pence' of medicine here."

Abstracts

THE CONTROL OF LOBAR PNEUMONIA.

By Frank L. Horsfall. *Canadian Public Health Journal, Vol.* 28, *No.* 10, *Oct.*, 1937, *p.* 476.

Pneumonia is now known to be the cause of more deaths than result from any other acute infectious disease. In Canada, at least 7,000 Canadians die each year of lobar pneumonia.

The prevention of lobar pneumonia depends partly upon the control of the upper respiratory infections which so frequently precede it. As yet, only the general measures of isolation are applicable in this respect. Despite extensive investigations it is not yet possible to assess accurately the value of active immunization against pneumococci. The rationale of the isolation of cases of lobar pneumonia is based upon the great rarity with which type I or II pneumococci are found in the throats of normal persons while from 15 to 25 per cent. of persons in contact with patients suffering from type I or II pneumonia become temporarily carriers of these virulent organisms.

The existence of at least thirty distinct and different types of pneumococci distinguished by their serological reactions has been thoroughly established. The basis of type-specificty has been shown to depend on the specific soluble polysaccharides in the capsules of virulent organisms. The value of type-specific antisera in the treatment of experimental pneumonia in animals has been definitely proven. It seems logical to assume that type-specific antisera should likewise cure lobar pneumonia in human beings.

Wherever the fundamental principles of specific serum therapy have been strictly adhered to, the results in humans have been excellent. That is, wherever typing has been carefully and rapidly done and type-specific serum of proper potency has been given in adequate amounts, the therapeutic effectiveness of antiserum has been proved. The degree of this effectiveness is inversely related to the duration of the disease at the time serum is given. It has been conclusively demonstrated that the use of serum materially shortens the duration of the disease and definitely reduces the mortality rate. Type I antiserum has been most extensively used with excellent results, and it is now established that types V, VII, and VIII antisera are also of very real value. Type II has also been successfully used although the results are not as encouraging as in the types already mentioned.

Although the accurate and rapid typing of pneumococci is a relatively simple procedure, it requires a certain technical training and in the best interests of the successful approach to the problem of controlling lobar pneumonia it seems wisest that typing be done in laboratories suitably equipped for the purpose.

Serum reactions, although unpleasant, are unimportant in the main. Chill reactions are not important and their incidence has been considerably reduced since the introduction of a concentrated anti-serum. Anaphylactoid reactions may be avoided by the use of conjunctival and skin tests for sensitivity. If these tests are negative, if the injection of serum is begun slowly and if epinephrine is at hand and is used immediately upon the development of untoward symptoms, then there is almost no reason to fear a serious reaction. Serum sickness occurs as a transient and unimportant sequel to serum therapy in 25-50 per cent. of cases. Urticaria, arthralgia and slight fever may occur but are never serious.

Calculating on the basis of the known percentage distribution of types of lobar pneumonia, it is seen that approximately 58 per cent. of all cases of this disease in the United States could have been treated had five type-specific sera been available. These cases contributed 57.4 per cent. of the total mortality of lobar pneumonia. On the average, these five types have, when not serum treated, a mortality of 31 per cent. With adequate serum therapy it is conservative to state that the average mortality in this group can be reduced to 12 per cent. or less. On this basis we arrive at the surprising total of 35,000 wholly unnecessary deaths from lobar pneumonia each year in the United States. The administrative and economic obstacles to the widespread use of anti-pneumococcal sera must be overcome. R.A.M.

PRONTOSIL IN THE TREATMENT OF GONORRHOEA

By T. F. Crean, *Lancet, Oct.* 16, 1937, *p.* 895.

In summarizing his results the author makes the following conclusions:

1. Treatment with Prontosil Soluble and sulphanilamide, combined with irrigations, proved efficient in 90 out of 100 cases of acute gonorrhoea, acute and chron-

ic. In favourable cases of acute gonorrhoea cure is obtainable in about 15 days.

2. Bad health, giving rise to poor resistance in the patient, is an adverse factor to cure by any form of treatment, including treatment with prontosil.

3. The dosage of prontosil should be adjusted to the needs of the individual patient, and other forms of treatment used as the occasion demands.

4. The shorter the time between infection and start of treatment the greater the success of prontosil therapy. Cases which failed to report, or had been unable to get efficient treatment for 15-20 days after infection, did not react as well to prontosil as cases which were treated within five days in infection.

5. It has been noted that cases which do not react to prontosil therapy within 18 days are not likely to react at all. It appears that the patients reach a stage where no further advance is made, and the power of reaction to other forms of treatment is adversely affected. The dosage, therefore, should be limited to 40 c.cm. of the prontosil soluble together with 13 oz. of colsulanyde over a period of 15 days.

6. A review of the cases treated suggests that prontosil will revolutionize the treatment of gonorrhoea. It has reduced the days' sickness to one-third, and from the economic point of view, has proved its value over and over again.

Reviewer's Note — Prontosil is being given an extensive trial at the Special Treatment clinic, T. G. H., and Dr. David Mitchell unofficially reports that it is proving to be the most useful therapeutic agent so far used, and that over 85% of cases of acute gonorrhoeal urethritis in males are cured within a short time.

J. D. D.

COMMUNITY PROVISION FOR THE SERUM TREATMENT OF PNEUMOCOCCIC PNEUMONIAS.

REPORT OF THE COMMITTEE ON PUBLIC HEALTH RELATIONS OF THE NEW YORK ACADEMY OF MEDICINE BY CECIL ET AL. *J.A.M.A. Vol.* 109, *No.* 17, *October* 23, 1937, *p.* 1323.

"Pneumonia is not only a very prevalent but a very deadly disease, the combined average lethal rate is about 25 per cent. and pneumonias occupy third place in the mortality bills of New York City."

Estimating 95 per cent. of the lobar and 75 per cent. of the bronchopneumonias as being due to pneumococci, the importance of the subject of this paper is realized. The curative value of concentrated specific immune horse serum has been established for the pneumonias of types I and II and evidence is rapidly accumulating that it is also efficacious in types V, VII, VIII, and XIV, but the general introduction of specific serum therepy has been slow due to lack of facilities and high cost of serums. There are now recognized some thirty-two types of pneumococci for each of which antisera can be prepared. The relative incidence of the various types varies somewhat from season to season but the common invaders in children seem to ba types I, VI, XIV, and XIX (New York City) and in adults, types I, III, VIII and V.

Taking up the problem in 1917, the Massachusetts Dept. of Health is now distributing serum of types I and II and will soon be distributing types V, VII and VIII, free of charge but subject to two restrictions.—

1. Laboratory report must indicate the infection is one of these types.
2. Patient must have been ill not more than four days.

In New York State, also, the serums are given away entirely free to all classes of patients. The actual cost of production of the serum is about 35 cents per 1,000 units or about 35 dollars per patient is the dosage used. It is hoped that the use of rabbit sera may lower this production cost.

Among the recommendations made by this committee are:

1. Education of physicians to the importance and mode of use of these sera together with establishment of free facilities for rapid determination of the type of infection.
2. Isolation of pneumonia in hospitals as a readily communicable disease.
3. Concentrated serum for the prevailing types of pneumonia readily available without cost to physician on request, provided type has been ascertained prior to request.
4. The results obtained in New York and Massachusetts justify the appropriation of funds for pneumonia control work and continued research.

A. F. G.

SULPHANILAMIDE IN THE TREATMENT OF GONORRHOEA

By ORR. HAROLD. O.B.E., M.D., D.P.H., F.R.C.P. *C.M.A.J., Oct.*, 1937. *Vol.* 37. *No.* 4. *p.* 364.

Sulphanilamide has proven a valuable therapeutic agent in the treatment of haemolytic streptoccal infections, meningococcic infections and more recently in gonococcal infections. This paper reports the results of its use in the treatment of 134 patients with gonococcal infections of the genito-urinary tract treated in the Provincial Government Clinic, Edmonton.

Toxicity—All of the 134 patients toler-

ated 80 grains of sulphanilamide daily for four days without ill effect. Six of the patients developed a sensitivity to sunlight which produced an acute urticarial eruption on the exposed skin. All the patients were conscious of a drug effect which varied from a slight feeling of dizziness or lassitude to a definite inability to do work which required mental concentration. Complete blood counts were done on more than one hundred of the patients and no changes attributable to the treatment were noted.

Absorption and Excretion—When large amounts of sulphanilamide are administered daily in divided doses, nearly 100% may be recovered from the urine when equilibrium between intake and output is established. It takes two or three days to establish this equilibrium and the same time to free the body of the drug after equilibrium between intake and output is established.

Clinical Observations—The series of cases was made up of 30 females and 104 males in various stages of the disease. The treatment consisted of:

(1) 80 grains of sulphanilamide daily for the first four days and 20 grains for the next seven days. The daily dose was given in four equal portions given every four hours from 8.00 a.m. to 8.00 p.m.
(2) Each patient was instructed to drink large quantities of water and milk; all other juices were prohibited.
(3) No local treatment of any kind was administered to these patients.

Determination of a cure in the male was based on the absence of gross pus or shreds in the first and second glasses of urine and by the demonstration of not more than eight pus cells per oil-immersion field, in the prostatic fluid; in the female by a series of not less than ten negative daily smears from the urethra and cervix.

Of the total of 134 cases 87.3 per cent. were cured, the percentage being about the same in the two sexes. Apparently sulphanilamide is of outstanding merit in the treatment of gonococcal infections.

R. A. M.

OBSERVATIONS UPON THE EXPERIMENTAL AND CLINICAL USE OF SULPHANILAMIDE IN THE TREATMENT OF CERTAIN INFECTIONS

By Long, P. H., and Bliss, E. A., *C.M.A.J.*, *Vol.* 37, *No.* 5. *Nov.*, 1937, *p.* 457.

Experimental—Experiments upon mice indicated that treatment with sulphanilamide is effective in controlling Cl. Welchii infections in these animals. In this connection it is noted that Bohlman has treated 5 patients suffering from gas-gangrene infections with sulphanilamide with good results in each case.

Clinical Observations Upon the Use of Sulphanilamide in Treatment of Certain Infections of Infancy and Childhood

In severely ill infants, sulphanilamide is best given by the parenteral route. Because of the frequency with which acidosis develops during treatment, the use of one sixth molar sodium lactate or Hartmann's solution as a solvent is recommended.

In other infections of infants in which sulphanilamide is used, the chemical may be added to their formulas. Care must be taken however that enough alkali is added to maintain the acid-base equilibrium. The effective blood level of sulphanilamide is 10 mg. per cent and to maintain this a dose of about 0.15 g. of the drug per kilogram of body weight is required.

A series of cases were presented in which sulphanilamide was used with excellent results in the treatment of diseases of children. Erysipelas, meningococcal arthritis, haemolytic streptococcal laryngitis and haemolytic streptococcal meningitis are included in the series. The results are quite impressive.

It is suggested that sulphanilamide will be an effective prophylactic agent in the prevention of the spread of epidemics of haemolytic streptococcal infections. In small children 92.5 three times a day in adolescents, twice that amount would constitute a prophylactic dose.

The Toxic Effects of Sulphanilamide—Mild dizziness, anorexia and nausea may be complained of especially if the patient receiving sulphanilamide is ambulatory. Cyanosis has been noted in 90% of the patients treated with sulphanilamide. The mechanism of its production is unknown and it is not regarded as an indication that treatment should be discontinued. Practically every patient who receives sulphanilamide in therapeutic doses shows a fall in the CO^2, combining power of the blood. This may be prevented by administering 10 grains of sodium bicarbonate with each dose of sulphanilamide given by mouth and by the use of sodium lactate as a solvent for sulphanilamide given parenterally.

There is no evidence that the drug causes renal irritation. However, its excretion is delayed in cases of damaged kidneys and in these cases the level of sulphanilamide in the blood must be carefully followed to prevent overdosage.

Four patients receiving sulphanilamide have developed acute haemolytic anaemias and one developed a marked leucopenia during treatment. Obviously the effect of the drug upon the blood should be carefully followed. In the case of anaemic patients it should be used only with extreme care.

In patients suffering from the acute

toxic manifestations of sulphanilamide, large amounts of fluid are an effective antidote. R. A. M.

PULMONARY EMBOLISM

By Arlie R. Barnes, M.D., *J.A.M.A., Vol.* 109, *No.* 17, *Oct.* 23, 1937, *p.* 1347.

The sudden and all too common tragedy of pulmonary embolism, accounting as it does for 3 per cent to 7 per cent of all hospital deaths, is discussed from several aspects. The most important predisposing factor yet known in its etiology is impaired circulation and in particular impaired venous return flow from the legs. In this, factors of age, obesity, cardiac disease, operation (especially abdominal) play a part. The sites of origin of the embolus would appear to be in order of frequency the iliac veins, femoral veins, pelvic veins, prostatic plexus, vena cava and right auricle. The author points out that in many cases the fatal embolism is preceded by one or more minor but premonitory attacks and that it is important to recognize these. Hence, in the diagnosis of pulmonary embolism, we must not wait for the cardinal signs of cyanosis, dyspnoea, pain in the chest and subsequent signs of pulmonary infarction but must regard as a common picture of acute pulmonary embolism, shock with or without dyspnoea, with faintness, pallor, sweating, acceleration of the pulse, a marked fall in blood pressure, vomiting and sometimes collapse. An electrocardiogram will also assist in diagnosis. The actual mechanism of death in fatal cases of pulmonary embolism is suggested to be a sympathetic inhibition and reflex arterial spasm rather than simply embolic occlusion of a pulmonary artery. Hence, the importance in cases which have shown a premonitory attack of having a syringe with ½ gr. of papaverine hydrochloride or other antispasmodic ready at hand, as well as morphia and perhaps instruments for performing a Trendelenburg operation.

The most important question dealt with by the author is, of course, that of *prevention.* Here the most promising avenue of attack is the attempt to improve the rate of circulation and particularly the velocity of venous return from the lower extremities. A comprehensive programme to this end should be applied at least *to those patients whose condition presents circumstances which are known to predispose to the occurrence of pulmonary embolism.* Among the measures applicable in such a programme may be mentioned in addition to other general systemic measures, the use of Trendelenburg position for 24 hours post-operative. Carbon dioxide inhalations several times during the first 48 hours. Deep breathing exercises. Keeping legs warm during and after operation. Frequent massage of legs during first 48 hours and twice daily thereafter. Passive and active movements of lower extremities at stated intervals. Administration of thyroid extracts is claimed by some to be of definite value. (In reading this article there comes to mind the work now in progress in Toronto on the use of heparin in this connection.)

A. F. G.

THE DEGREE AND PREVALENCE OF VITAMIN A DEFICIENCY IN ADULTS

By Harold Jeghers, M.D., *J.A.M.A. Vol.* 109, *No.* 10, *Sept.* 8, 1937, *p.* 756.

Do you grope your way to a seat in a darkened theatre? Do headlights glare for you at night? Perhaps you are suffering from a vitamin A deficiency. In a survey of 125 medical students Dr. Jeghers found that 35% showed some evidence of such deficiency as shown by photometric measurements of the visual purple content of their eyes. 12% showed clinical manifestations of deficiency: night blindness, photophobia, dry skin, dry conjunctivae, blepharitis and follicular hyperkeratosis. Analysis of the factors producing this deficiency showed that the skipping of meals and poor choice of foods were chiefly responsible. Infections were more numerous and severe among the deficient students. A vitamin A deficient diet was employed to produce deficiency manifestations experimentally in the author who in common with the deficiency cases above mentioned, responded quickly to vitamin A therapy in the form of carotene in oil or haliver oil. Interesting case histories, and vitamin A content of most foodstuffs are given in this article. The author concludes that 4,000 international units of vitamin A is the minimum daily requirement for a healthy adult. Evidence is obtained that it is dangerous for a hemeralope to drive an automobile at night.

A. F. G.

SYMPOSIUM ON ANTERIOR POLIOMYELITIS

Presented at a special meeting of the Academy of Medicine, Toronto, September 7, 1937, *and reprinted in Canadian Public Health Journal Vol.* 28, *No.* 9, *Sept.* 1937, *p.* 417.

An extremely interesting and valuable summary of present knowledge of anterior poliomyelitis is presented by a variety of authors. It should be carefully read by every medical student. Included in this symposium are:

(1) Present Incidence of Poliomyelitis in Ontario.—J. T. Phair.

(2) Poliomyelitis: Virus and Experimental Infection.—J. Craigie.
(3) Some Epidemiological Features of Poliomyelitis.—R. D. Defries.
(4) Symptomatology.—Beverley Hannah.
(5) Difficulties in Prognosis.—Nelles Silverthorne.
(6) Nasal Spraying as a Preventive of Poliomyelitis.—F. F. Tisdall.
(7) Convalescent Serum Therapy.—N. E. McKinnon.
(8) The Surgical Treatment of Polioyelitis During its Early Stages.—Surgical Staff, Hospital for Sick Children.

Every medical student or practitioner should become well acquainted with the facts presented in these articles.

R. A. M.

ATHLETIC INJURIES OF THE KNEE JOINT EXCLUDING CARTILAGE INJURIES

By W. E. Tucker, B.Ch., F.R.C.S., Orthopaedic Surgeon, London Homeopathic Hospital. *Brit. Med. Jour., Sept.* 11, 1937, *p.* 525.

Of all athletic injuries those to the knee joint are most common and often lead to prolonged unnecessary incapacity. Yet the athlete is usually a sane person who can aid much in his own treatment if the latter is explained to him.

Such injuries may be divided into those due to (a) direct violence (b) indirect violence.

Direct violence may cause:

(1) traumatic synovitis
(2) contusion of the quadriceps or its expansions, often followed in a few days by a synovitis from blood seepage
(3) prepatellar bursitis or infrapatellar fat bruising
(4) fracture of patella or head of fibula

Therefore, if tenderness near a bone, x-ray should be used.

Indirect violence may be:

(1) flexion, producing synovitis
(2) rotation, if mild, causing synovitis; if severe causing cartilage injury
(3) lateral wrenches, injuring lateral ligaments
(4) extension, injuring ant. cruciate ligament, infrapatellar fat and allar folds, posterior capsule structures and popliteus tendon.

For all injuries it must be stressed that graduated remedial exercises are essential and examples of such exercises are given.

Internal Lateral Ligament Spasms.

Caused by abduction wrench, are one of commonest of injuries to knee. If rotation is associated the internal cartilage is also injured but this is uncommon in athletic injuries. Signs of ligament sprain are marked tenderness at upper or lower end and external rotation is limited and painful. A flake of bone may be detached and x-ray should always be used. If *early* after injury, there is no complication such as a damaged cartilage, extension is *not* limited. Later if relaxed, injured ligaments tend to shorten and limit extension.

(a) Mild degree
Heals in 6 days; treat by faradic stimulation of quadriceps, passive movement of knee joint, diathermy and rest.
(b) Moderate degree
Heals in 6 weeks; treat in plaster for variable time, knee in full extension with patella uncovered and moved each day; otherwise as in (a)

External Lateral Ligament Sprains

Often associated with sprains of biceps tendon, iliotibial band and ext. quadriceps expansion. Swelling of a cystic nature and tenderness are chief signs.

Treat by heat, massage, graduated faradic contractions and gentle manipulations. X-ray eliminates fractures of head of fibula.

Infrapatellar Fat Pad and Alar Fold Bruising

Signs are swelling and tenderness below patella and on each side of patellar ligament, limitation of full extension and pain on coming downstairs. Quadriceps tends to waste early and allow more swelling under patellar ligament.

Treat by massage, faradic stimulation of quadriceps and diathermy. If ant. cruciate ligament is involved, the treatment is plaster cast for 3 weeks with faradic stimulation of quadriceps.

Synovitis

May complicate all above conditions.

Treat by aspiration followed by firm bandage with heat, massage, faradic stimulation. No weight-bearing while effusion is present. If not cleared in one month, must search for underlying septic focus.

Chronic Knee Strain

Seen in older, overweight patients following prolonged exercise. Signs of synovitis, atony of quadriceps and limitation of extremes of movement are present.

Treatment is heat, massage, graduated muscular contractions with limitation of active exercises. Treatment must be maintained to prevent osteo-arthritic changes.

Quadriceps Insufficiency

Common cause of recurrent synovitis or unstable knee. Often mistaken for torn cartilage.

(1) Vastus Internus Insufficiency — Pain and strain on inner side of knee.
(2) Crureus and Subcrureus Insufficiency—Symptoms referred to infrapatellar pads and alar folds.
(3) Vastus Externus Insufficiency — Pain and instability of outer side of joint with wasting of quadriceps. Often mistaken for ext. cartilage injury.

Treatment is graduated exercises. If any limitation of movement, there must be a forcible manipulation of the joint.

Conclusion

(1) Severe sprain of int. lat. ligament recovers slowly and treatment cannot be forced.
(2) Quadriceps insufficiency may be divided into three parts, inner, middle and outer.
(3) Forcible manipulation of knee joint before labelling it functional or before removing a doubtful cartilage.
(4) Always give the patient remedial exercises.

J. A. G. R.

SYMPOSIUM ON PEPTIC ULCER.

Surgery. Vol. 2. No. 5. Nov., 1937.

Physiology of Peptic Ulcer.

By Michael DeBakey

The author postulates that certain factors play important roles in the etiology and pathogenesis of peptic ulcers.

1. *Constitutional.*

Existence of an inherent factor predisposing to the development of an ulcer cannot be denied, the so-called "Ulcer Constitution."

2. *Chemical.*

Some abnormal inability of the alkaline duodenal juices to neutralize the normal or probably hyperacid gastric secretion. Normal acidity was found in 1/3 cases and hyperacidity in approximately ½ of cases.

Ochsner and his co-workers have expounded the theory that maintains that ulceration is established by the summation of two groups of factors.

1. *Predisposing*, which may be considered to be uncontrollable in that they are inherent.

(a) The Constitutional factor as mentioned above.
(b) Tissue Susceptibility in that certain portions of the G. I. Tract possesses an inherent vulnerability to be digested by the acid gastric juice. These areas are mainly the lesser curvature of the stomach, the duodenal cap and jejunum. This innate character is present in all individuals.

2. *Precipitating*, which are controllable or can be modified.

(a) Chemical. Disturbances of the normal physiological relationship between the acid gastric juice on one side and the alkaline duodenal juices on the other, with hypersecretion and hyperacidity as important contributing factors.
(b) Mechanical or Traumatic. Effect of rough foods and gastric retention which results from pylorospasm or achalasia which is conducive to hyperacidity and prevention of alkaline duodenal regurgitation.
(c) Infection. May act directly, causing specific inflammatory changes or indirectly where some focus of infection causes pylorospasm and gastric retention.

Pathology of Gastric Ulcer.

By J. H. Dible, Liverpool.

The pathology of ulcer is set forth in plain, straightforward manner. It clearly states the gross and microscopic pathology along with common complications of the disease, such as perforation, haemorrhage, stenosis and malignancy.

Value of Gastroscopy in the Diagnosis and Surgical Treatment of Chronic Gastroduodenal Ulcer.

1. Reveals gastric ulcers not demonstrable by other means.
2. Success of the Medical Treatment can be ascertained.
3. Extent of inflammation accompanying the ulcer may be seen and thus form a decisive indication for operation.
4. Will reveal the source of gross haemorrhage.
5. Recurrent marginal or duodenal ulcers postoperatively, can be determined.
6. Less important factors, e.g., can see whether the artificial stoma is efficient, postoperatively.

A short article gives the indication for operative treatment from the standpoint of relieving symptoms only, and from the standpoint of eliminating the ulcer.

The remaining papers of the Symposium deal with:

1. "Acute massive haemorrhage from the upper G. I. Tract."

2. "Surgical Treatment of Ulcer by Conservative Measures." (By Donald Balfour).
3. "Pyloroplasty and Gastroduodenostomy. Technique and Indications."
4. "Should Gastric Resection be done for Duodenal Ulcer?"

The papers are all written by excellent men and the reviewer can recommend these articles highly for their wealth of material and literary style. The magazine in which these articles are contained, is a new and welcome addition to the already growing list of Medical and Surgical magazines. With such outstanding men as Dean W. E. Gallie and Dr. Roscoe R. Graham, of our Medical Faculty, on the advisory and editorial boards, we are assured of a fine Journal.

E.B.T.

PEPTIC ULCER OF MECKEL'S DIVERTICULUM.

By W. I. Card and T. W. Mimpriss. *Lancet, October* 23, 1937. *p.* 963.

Cobb (1936) has collected 100 probable cases of peptic ulcer of Meckel's diverticulum. Gastric mucosa has been found in the diverticulum of 66 of these; the remainder were not examined histologically. Of the 66 cases, 9 were in females. Perforation of peptic ulcer has occurred in 32 of these proved cases; only 3 were in females. This preponderance in males appears to be highly significant. When it is considered that the condition usually occurs in childhood at a time when general living conditions and diet are very similar for the two sexes, the female seems to enjoy an especial freedom from ulceration depending solely on her sex. However, no control observations are available. We therefore cannot infer a relative immunity of the female to this type of peptic ulceration since Meckel's diverticulum is twice as common in males, and we can find no figures to show the relative incidence of gastric mucosa in normal diverticula in the two sexes.

The commonest presenting signs of an ulcer of Meckel's diverticulum are severe rectal haemorrhage, or perforation. Of the 100 cases collected by Cobb, 71 had had haemorrhage, 53 had perforated, 35 had had haemorrhage followed by perforation while in the remainder the ulcer was only found at operation or autopsy. The cases likely to be missed are those in which bleeding is the presenting sign and the condition should certainly be considered as a cause of rectal haemorrage especially in children. Even if an ulcer of Meckel's diverticulum is suspected it is difficult to demonstrate the diverticulum by radiography, though this has occasionally been done Case (1926) appears to have been the first to demonstrate a diverticulum that was afterwards confirmed by operation. If an ulcer may reasonably be suspected from the history of repeated rectal haemorrhages, and a complete physical and radiological examination is negative, we feel that it is justifiable to advise laparotomy in view of the risk of further haemorrhages or perforation. J.D.D.

THE SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM.

By J. R. Learmonth. *The British Journal of Surgery. Vol.* 25. *No.* 98. *October,* 1937.

The results of Sympathectomy depend on the permanence of interruption of nerve pathways, on the presence of a local nervous apparatus which can restore and maintain physiological control, and on the stage of the disease which necessitates sympathectomy. Difficulties arise from the lack of a consistently uniform anatomical arrangement, from the tendency to employ Sympathectomy as the sole remedial procedure, and from the practical difficulty of separating small structures in difficult situations.

Excision of the Superior Cervical Ganglion has been done to approximate the eyelids in cases of long-standing facial paralysis, and to increase the blood supply to the face after section of the Fifth root. Leriche uses Stellatectomy in the treatment of Angina Pectoris but most Cardiologists do not agree with him that the operation interrupts the vasoconstrictor reflex, the afferent pathways for cardiac pain, and the coronary vaso-constrictor nerves, but in a series of 24 cases Leriche did not have one case of "sudden death."

In the Upper Extremity pre-ganglionic section is used while in the Lower Extremity the operation is done by either an extra—or intraperitoneal approach and a spinal anaesthetic is used. Patients are selected by first testing their power of vasodilatation. Raynaud's Disease, Buerger's Disease, Hyperidrosis, Hyperpiesia, Arthritis are definitely benefitted. It is also used to modify visceral function of Alimentary or Urinary tract, and to relieve pain.

A.G.M.

ARTERIOLAR SCLEROSIS IN HYPERTENSIVE AND NON-HYPERTENSIVE INDIVIDUALS.

By Alan R. Moritz, M.D., and M. R. Oldt, M.D. *American Journal of Pathology. Vol.* 13. *Sept.,* 1937. *p.* 679.

Three divergent views have existed as to the pathogenesis of chronic (essential)

hypertension. 1. that the renal disease is primary; 2. that the renal disease is part of a diffuse vascular disease; 3. that the renal and vascular changes are secondary and the hypertension is primary. The determination of the relation that arteriolar disease bears to chronic hypertension is of more than academic interest since the advent of surgical treatment. If the organic changes are primary, less can be expected of operations designed to relieve vascular spasm than if the vascular spasm were primary and the organic changes secondary. These authors from the evidence presented, draw the conclusion that renal arteriolar sclerosis is primary and the hypertension is secondary, since the kidneys were the only organs in the body where the presence of arteriolar sclerosis is almost invariably associated with hypertension and the absence of arteriolar sclerosis betokened an absence of hypertension. They point out that no evidence has been brought forward to suggest that the renal vessels are more sensitive to changes in blood pressure than are arterioles in other organs, which must be assumed if the hypertension is primary.

The histology of arteriolar sclerosis is also described. There are three types: 1. intimal hyalinization, which is the counterpart of the degenerative changes of arteriosclerosis; 2. medial hypertrophy following stretching of the wall and being most frequently encountered in hypertension; 3. intimal proliferation seen in endarteritis obliterans, in parenchymatous physiological atrophy (e.g. uterus), or in primary vascular inflammation. Excellent coloured plates appear at the end of the article.

W.G.R.

THE AIMS OF PSYCHIATRY

By J. A. Kindwell, *Mental Hygiene, Vol.* 21, *No.* 3.

An attempt is made here to present a rather broad conception of the purpose of psychiatry in the scheme of things therapeutic and sociological. Since the depth of the article is somewhat limited by its scope, there is no involved discussion of opposing hypotheses and it forms a bit of really worthwhile reading, particularly for those students whose active interests in psychiatry extend little further than the prescribed courses. The concise, though necessarily limited compilation of the factors predisposing to mental instability should prove valuable.

Psychiatry is aptly described as an art, resting on a still developing science and still largely dependent upon the psychiatrist's personality and the personal relationship he develops with the patient.

The relationship between personality make-up and inherent (or inherited) tendencies and environmental influence is presented in a pleasant dress with only a passing reference to Mendelism and without the always boring and usually irrelevant statistics. The conflicting requirements which modern civilization makes upon man are neatly summed up, with their effect upon those individuals who fail to distinguish when to inhibit and when to let go and whose activity is frequently reduced to a symbolism which may be meaningless to both observer and patient.

There is also a brief summary of the major psychoses, both "functional" and "organic" and of the milder psychoneuroses with their possible significance to society. Here, the author considers the latter group of greater import because of the fact that its sufferers frequently reach positions of high station where their psychoneurotic mechanisms might affect whole peoples.

The integrative role which the psychiatrist should play in both diagnosis and treatment is briefly developed.

G.D.T.

THE RELATION OF ELECTROCARDIOGRAPHIC CHANGES TO THE ARTERIAL CONCENTRATIONS OF OXYGEN, CARBON DIOXIDE, AND CYCLOPROPANE IN DOGS ANESTHETIZED WITH CYCLOPROPANE

By Robbins, B. H., and Baxter, *J. H.* J. *Pharmacol. and Exper. Therap.* 61: 162 (1937).

Experiments were undertaken to investigate the cause of cardiac arrhythmias, e.g. extrasystoles, multiple focus ventricular tachycardia, occurring under cyclopropane anesthesia. Dogs were anesthetized with a 30% to 40% mixture of cyclopropane in oxygen. Analyses were made of blood O^2, CO^2, and cyclopropane, and heart rates and electrocardiograms were taken at the start of each experiment, at the stage of surgical anesthesia, at the occurence of respiratory failure, and at the occurrence of cardiac arrhythmia.

The results so obtained indicate that the heart is not adversely affected until the concentration of blood cyclopropane has reached the point of stopping respiration or so diminishing it as to cause severe anoxemia, even though the anesthetic mixture in the bag contains sufficient oxygen. Under artificial respiration it was possible to build up a 30% higher blood cyclopropane concentration without cardiac arrhythmia. Beyond this point, however, cardiac arrhythmias and failure result, probably due to direct action of the drug on the heart.

It is believed that the cardiac arrhythmias which develop at the time of or

soon after respiratory failure are not due to cyclopropane but to anoxemia.

F.L.L.

FUNCTIONAL ACTIVITY AND pH OF THE CEREBRAL CORTEX

By Dusser de Barenne, J. G., McCulloch, W. S., and Nims, L. F. *J. Cell & Comp. Physiol.* 10: 277 (1937).

Simultaneous recordings of the pH of the cortex and electrocorticograms were taken by elaborate and very accurate methods. The following results were obtained:

(1) Hyperventilation of the animal (monkey), by removing CO^2 from the blood, causes an increase in the cortical pH.

(2) Hypoventilation of the curarized animal, resulting in accumulation of CO^2 in the blood, leads to a decrease of the cortical pH.

(3) In hyperventilation, the increased cortical pH is associated with an increase in the spontaneous electrical activity of the cortex. With the decreased cortical pH of hypoventilation, the cortical action potentials are reduced.

(4) The level of electrical activity of the cortex is determined largely by its pH, whatever the manner of producing that pH. This is shown by the intravenous injection of weak alkali or acid.

(5) Increased pH of the cortex results in a marked increase in its excitability, whereas decreased pH is associated with decreased excitability. These changes in excitability hold for both cortex and lower centres, and for neural as well as electrical excitation.

(6) Cortical after-discharge, following either neural or electrical excitation, is associated with the development of a local acidity (decreased pH) sufficient to account for the subsequent decrease in cortical action potentials.

(7) Stimulation of those cortical areas which control respiration and autonomic functions produces alterations of pH and excitation which complicate the picture.

F.L.L.

THE NATURE OF THE LIPOTROPIC AGENT IN PANCREAS

By Aylward, F. X., and Holt, L. E. *J. Biol. Chem.* 121: 61 (1937).

An attempt was made to throw some light on the question, whether choline is the sole lipotropic liver factor in pancreas. Analyses were carried out on the livers of four groups of rats, fed respectively: (i) a basal fatty-liver-producing diet; (ii) this diet plus choline chloride; (iii) the diet plus raw pancreas of equivalent choline content; (iv) the diet plus autoclaved pancreas of equivalent choline content. A small number of curative experiments were also carried out

The basal diet caused a change in the liver lipid content from the normal value of 6% to 30%. Animals receiving choline chloride or raw or autoclaved pancreas showed uniformly low liver fat analyses. In the curative experiments pancreas was no more active than would be expected from its choline content.

In summary, the experimental results gave no indication of a lipotropic factor in pancreas other than choline, as far as the alimentary fatty liver of the rat is concerned.

F.L.L.

EVIDENCE OF THE PROTECTIVE INFLUENCE OF ADRENAL HORMONES AGAINST TUBERCULOSIS IN GUINEA PIGS

By E M. Pottenger and J. E. Pottenger. *Endocrinology. Vol.* 21; *No.* 4; *July,* 1937, *p.* 524.

Previous work has shown that rats—a species normally very resistant to tuberculosis—are rendered susceptible by adrenalectomy. In these experiments, guinea pigs were injected intraperitoneally with approximately 100 tubercle bacilli, obtained from fresh human sputa. The criterion of infection was recovery of tubercle bacilli from the tissues at autopsy, together with gross lesions when present.

Of 23 inoculated controls, all became infected, while of 43 animals similarly inoculated, but also treated with adrenal cortical extract, 12 (28%) showed no evidence of tuberculous infection and in the remainder, the involvement was milder and less extensive.

D.H.C.

TRANSMISSION AT NERVE ENDINGS BY ACETYLCHOLINE

By G. L. Brown. *Physiological Reviews. October,* 1937.

This article presents for the student of phsyiology and pharmacology a good review of the historical events that have led up to the knowledge we now possess of the transmission of nervous impulses by acetylcholine. There has been a great deal of interest in this field since the classical work of Loewi in 1921. But of much more practical value is the extremely lucid way in which the author has summarized the existing facts. He deals with

this under a number of headings which include a list and distributions of the cholinergic nerves, the muscarine and nicotine-like transmissions, transmissions at the neuromuscular junction and the storage and liberation of acetylcholine.

This is a subject that often presents difficulty to the student. The review, therefore, is of considerable value to him and is highly recommended for anyone who desires a concise but clear knowledge of this subject. M.E.H.

CHANGES IN BLOOD VESSELS WITH INFLAMMATION

By Ernest Zander. *Journal of Experimental Medicine. Vol.* 66; *No.* 5.

In the preamble, it is pointed out that a study of the changes in vascular walls favoring the escape of red blood cells is suggested by the occurrence of haemorrhage in association with many forms of inflammation. Capillary bleeding can be produced by altering the relation between extra and intra capillary pressure. Experiments are cited in which this was done by obstructing venous flow and noting the degree of capillary bleeding by the number of petechiae which appeared in the skin.

In this set of experiments, however, the investigator altered the extra-capillary pressure applying negative pressure (—70min Hg) to the skin of rabbits until uniform hemorrhage occurred over the area to which suction was applied. The time required (about 8 min) was taken as the index of capillarly fragility.

Local inflammation was produced by intracutaneous injections of a chemical irritant (turpentine in paraffin oil 1:50) and of killed bacteria. The time required to produce hemorrhage 30 minutes after injection was increased to ½ to 2 hours, indicating decreased capillary fragility. However, from 12 to 24 hours after injection, the period of suction necessary was only 1 to 4 minutes. Similar phenomena were observed in allergic inflammation by the use of sensitized animals but capillary fragility was found to be no greater than in unsensitized animals.

The subsequent course of events was found to vary depending upon the agent used to induce inflammation. Resistance of capillary wall to suction may return to normal in 2 to 9 days (turpentine and streptococci); may be elevated for some days (staphylococci and pneumococci); or depressed for a week or more (Old Tuberculin). G.D.T.

Book Review

THE BASIS OF CLINICAL NEUROLOGY

By Samuel Brock, M.D. *Wm. Wood and Co. Baltimore.* $4.75. 347 *pages.*

This book is another example of the present trend to regard disease in terms of physiological malfunction. The author sets out to present neuro-anatomy and neurophysiology from a standpoint of clinical usefulness.

He makes numerous references to comparative neurology but warns against drawing false conclusions from animal experimentation alone. Chapters III - IX deal with the spinal cord, ending with an excellent summary of the common lesions. Chapters X - XXIV present the Brain Stem and Cerebellum. The anatomical description is accompanied by numerous easily read diagrams. It may be mentioned here that a generous use of clear illustrations throughout greatly increases the value of the volume. The epithalamus and thalamus are given considerable attention. The section on the hypothalamus, that much blamed and little understood region, is a delight to one who is unable to keep abreast of the literature. The basal ganglia and pyramidal tracts are dealt with in some thirteen pages of easily assimilated writing. The nuclei are no longer to be remembered for examination purposes but are made tools for the student to use in elucidating signs and symptoms. This Chapter concludes with a summary of the views of each of the leading groups of workers in the field. The section on aphasia is of special interest. The author presents several theories, including one with an approach in terms of Gestalt Psychology.

The references in this book deserve special mention. They are sufficient in number to form a good guide to more detailed reading. What is more remarkable in a text book, they are recent. There seems to be only one criticism and that will probably be corrected in future editions. The index, particularly to the diseases, is not complete. Every student would do well to read and those aspiring to neurology would do well to possess, this volume so readably written. M.A.D.